Rogoff *et al.* treated four cases of peritoneal mesothelioma with intraperitoneal radioactive phosphorus and abdominal radiotherapy; three of them with some chemotherapy as well (619). Two patients survived more than 10 years, one was alive 2 years after treatment, and the fourth survived 1.5 years. [A]

Comment

The conclusions to be drawn from reports of treatment so far tried are disappointing. Not only are the results generally poor, but the various treatments have been applied in haphazard fashion and the reports are generally lacking in the detail which would permit systematic evaluation. It would appear most profitable at this juncture for two or three of the most promising regimens to be applied systematically to a series of cases under agreed protocols. To obtain a sufficiently large series for immediate treatment, the study would probably need to be organized on international lines. In the meantime, one must agree with Elmes that mesothelioma "is a disease in which prevention is far more effective than the cure (217)."

12

Characteristics, Etiology, and Prevalence of Asbestos-Associated Carcinoma

DEFINITION

The high prevalence of carcinoma in the population at large during the last three decades and the increased incidence of pulmonary carcinoma in particular are only too well known. Persons exposed to asbestos, like any other occupational group, share in this general risk but are open to any other carcinogenic factor peculiar to their environment. In what is coming to be recognized as a disease of multifactorial origin, any additional causative factors call for special investigation. It has become progressively clear, as will be seen later, that the appearance of pulmonary carcinoma in persons exposed to asbestos is significantly more frequent than that which may be expected from general population data. There is also some evidence that the prevalence of carcinoma in other bodily sites may also be greater than expected. (We will use the term "carcinoma" here rather than the simpler word "cancer" to make it clear that we are excluding mesothelioma and other neoplastic developments. Past use of the phrase "lung cancer" to include both carcinoma and mesothelioma sometimes led to confusion that we wish to avoid.)

For the purpose of our discussion we have defined asbestos-associated carcinoma as that which occurs in members of population groups that have been demonstrated to have an exposure to asbestos

Published by AsbestosClaims.Law
asbestosclaims.law/library/25349/1

significantly greater than that of the population at large. From what has been said in earlier chapters it will be recognized that such groups involve, not only those handling asbestos in their normal work, but associated trade groups—those who live or work in the neighborhood of asbestos plants, and the families of asbestos workers who are adventitiously exposed—whether or not we have data that will permit us to discuss their risk.

For these reasons, the development of carcinoma in those persons who are exposed to asbestos calls for special attention. In the earlier years of such considerations, there was a tendency to speak of the occurrence of carcinoma only in those who had demonstrable asbestosis, but it gradually came to be recognized that the increased risk could also apply to those who have been exposed but in whom frank fibrosis has not been demonstrated. On the other hand, we can hardly extend consideration to all those in whose lungs asbestos bodies or even fibers can be demonstrated by modern methods, since that could include a very large part of the general population, particularly in manufacturing cities. Unless otherwise indicated the following discussion will relate to pulmonary carcinoma.

SPECIAL FEATURES

The clinical and pathological picture of pulmonary carcinoma is so well known and described in standard texts that repetition here would be superfluous. But there are some features of the tumor associated with exposure to asbestos that call for description.

In a person who already has asbestosis, the prior existence of pulmonary symptoms may mask the onset of carcinoma. Increase in the intensity and persistence of cough, the addition of chest pain to a sense of restriction, and particularly the occurrence of hemoptysis would strongly suggest the development of carcinoma, as would anorexia and loss of weight which are not common in uncomplicated asbestosis.

While some authors speak of tumors appearing in the hilar region (226), our experience and that of many others is that a large proportion are situated in the peripheral portion of the lungs and may secondarily involve the pleura. All authors are agreed that, whereas the majority of pulmonary carcinomas appear in the upper portions of the lungs, those associated with asbestos appear more commonly in the lower lobes. The distinction is not absolute, however. Jacob and Bohlig were able to say by 1959 that the ratio of appearance in upper as contrasted with lower lobes in Dresden was 1/3.5 in persons with asbestosis, as against 2–2.5/1

in those without (374). Kiviluoto reported in 1965 that in Finnish cases with asbestosis, the carcinomas were equally distributed in upper and lower lungs, as against 96/40 in those without asbestosis (403). Another feature, which may be changing with changes in smoking habits, is the more frequent occurrence of pulmonary carcinoma in women with asbestosis than in those without. Some of this, no doubt, is due to the extensive employment of women in wartime industry.

With regard to pathology, experience at Mount Sinai suggests that there is no essential difference between pulmonary carcinoma in general and that associated with asbestos except the more frequent occurrence of the latter in the lower lobes, and possibly a tendency to involve and spread along the pleura, particularly by those tumors which are peripherally located (388). We have not found any real difference in the preponderance of various cell types, but Whitwell *et al.* reported a fairly high percentage of adenocarcinomas (34%), more characteristic of tumors in the distal airways, and suggested that this was consistent with a synergistic relationship between asbestos, whose effects are generally more noticeable there, and cigarette smoking, which can affect all airways (791). In a number of cases the tumor appears to have a multicentric origin (633). In the radiograph, preexisting parenchymal fibrosis may mask the earlier manifestations of a carcinoma. Some illustrative radiographs are given as Plate 12–1,a–e.

In those instances in which the tumor develops from an accessible bronchus, bronchoscopy may reveal the usual appearances of bronchogenic carcinoma and permit the taking of specimens for histological examination, especially with fiberoptic techniques; but tumors developing more peripherally may be beyond reach. Because of the risk of disseminating malignant cells, among other reasons, transthoracic needle biopsy is not recommended in operable cases (72). It has been reported that metastases to the abdomen from a primary tumor in the lung may be extensive and anaplastic; this may pose some difficulty in distinguishing it from a mesothelioma (246).

Treatment would be as for bronchogenic carcinoma in general, except that when surgical removal is considered, the coexisting embarrassment of remaining lung by asbestosis needs to be assessed and included in the clinical judgment of its advisability.

ETIOLOGY

The definition given above does not imply that every carcinoma that develops in some member of a designated group is necessarily due to

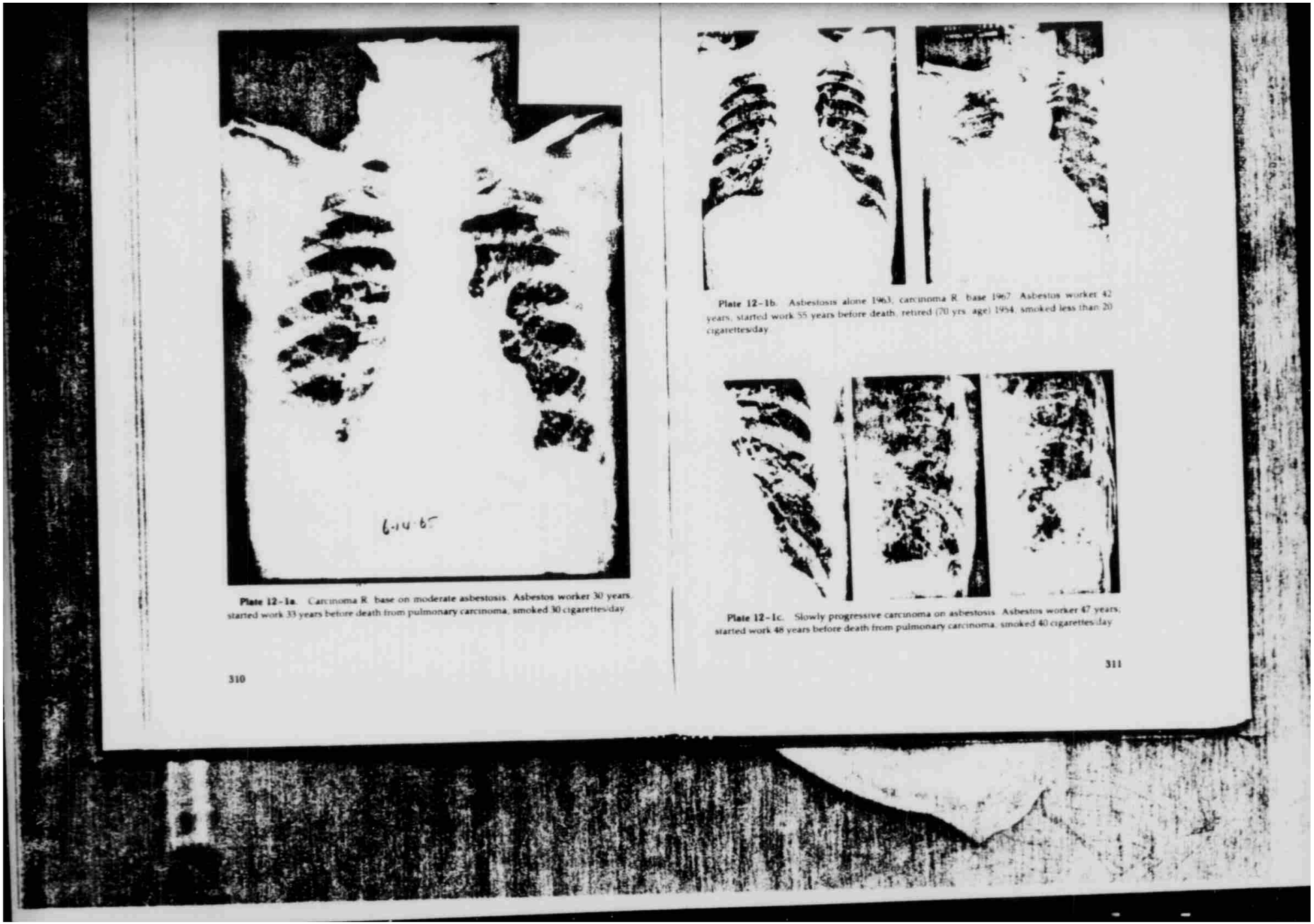


Plate 12-1a. Carcinoma R. base on moderate asbestosis. Asbestos worker 30 years, started work 33 years before death from pulmonary carcinoma; smoked 30 cigarettes/day.

Plate 12-1b. Asbestosis alone 1963, carcinoma R. base 1967. Asbestos worker 42 years, started work 55 years before death, retired (70 yrs. age) 1954; smoked less than 20 cigarettes/day.

Plate 12-1c. Slowly progressive carcinoma on asbestosis. Asbestos worker 47 years, started work 48 years before death from pulmonary carcinoma; smoked 40 cigarettes/day.

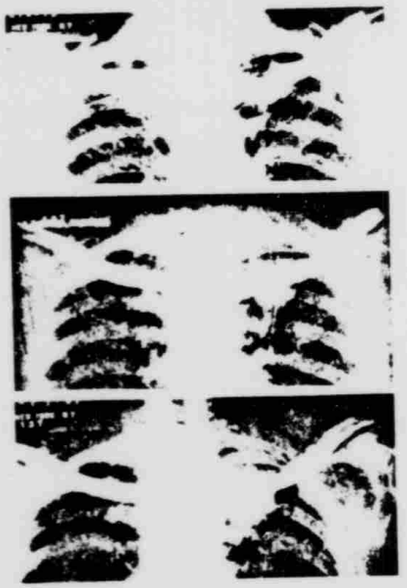


Plate 12-1d. Asbestosis alone in 1963; carcinoma L. hilum 1966. Asbestos worker 35 years, started work 47 years before death from pulmonary carcinoma; smoked 15 cigarettes/day.

the action of asbestos, many of them would have occurred if the person had never been so exposed. It is impossible to distinguish one from the other, but the simultaneous presence of asbestosis would certainly strengthen the probability of their being an etiological relationship. From what is about to be discussed, it will be seen that the risk of acquiring a carcinoma, particularly of the lung, is distinctly increased by such exposure and that the high probability of at least a cocarcinogenic action by asbestos must be taken into statistical account. The

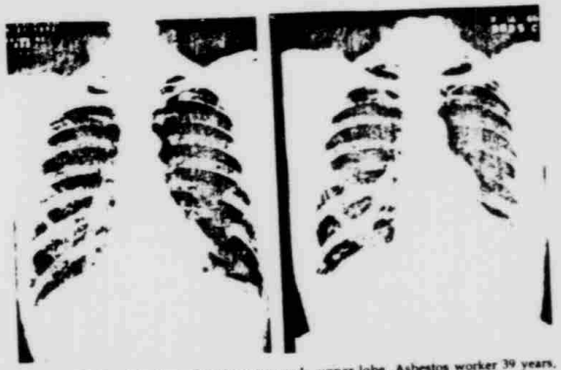


Plate 12-1e. Development of carcinoma L. upper lobe. Asbestos worker 39 years, retired (56 yrs. age) 1955. Death from pulmonary carcinoma 1967; smoked 20–30 cigarettes/day.

proposition will be examined in terms of the five criteria that were enunciated in Chapter 6.

Association between Exposure and the Syndrome (First Criterion)

The doubts and uncertainties about a causative relationship, from the first published description of a carcinoma in a grossly asbestotic lung by Lynch and Smith in 1935 through 1958, have been reviewed in Chapter 1 dealing with historical background. As early as 1941, Nordmann and Sorge gave reasons for believing that there was one (553). Three of their reasons have since been continually reinforced as data have accumulated: (1) that pulmonary carcinoma was appearing in 12–20% of autopsies on asbestos workers; (2) that the tumor was appearing in a younger age group (down to 35 years); and (3) that the lesion appeared mostly in the lower lobes instead of in the upper portions as was more usual in those not exposed to asbestos (553). In 1947 Merewether reported that he had found lung cancer in 31 out of 235 men (13.2%) with asbestosis who died between 1924 and 1946, as against 91 out of 6,884 (1.32%) with silicosis (509). Gloyne gave similar

data in 1951: 17 lung cancers in 121 asbestos workers with asbestosis (14%) as compared with 55 in 796 (6.9%) with silicosis (281).

In reporting a case of widespread squamous metaplasia of the bronchi in an asbestos worker in 1953, Isselbacher *et al.* reviewed the literature and found that of 603 deaths with asbestosis, 83 were due to carcinoma of the lungs—an incidence of 13.8%, which was considerably higher than that reported for routine autopsies (0.8 to 2.4%) (368). They also noticed a relatively high proportion of females in those affected, as compared with data on the general population. In 1955 Doll reported finding 18 cases of lung carcinoma in 105 men who died after working more than 20 years with asbestos, yielding a rate some ten times higher than that in the general population (192).

From that time on, the concept of a significantly increased risk of pulmonary carcinoma in workers with asbestosis has received increasing acceptance. By the time of the Conference on the Biological Effects of Asbestos, organized by the New York Academy of Sciences in October, 1964, very little opposition remained. Some nine papers at that meeting dealt with the problem, all supporting the association. There remained some doubt, however, as to whether there is an excess of lung cancer in persons exposed to asbestos, but who have not developed obvious parenchymal fibrosis (310).

Preliminary results from the cohorts established at Mount Sinai, strongly supporting the concept of asbestos-associated carcinoma, were given at that conference. The data through 1973 in Table 12–1 compare the observed deaths from various types of cancer with those expected on the basis of age-specific death rates for the United States provided by the National Office of Vital Statistics. It will be seen that in all four cohorts the death rate from pulmonary carcinoma is very much higher than would be expected from persons of similar age not employed in the trades indicated. Gastrointestinal carcinoma is also more common than would be expected, but not so markedly. The significance of this latter excess in any one cohort might be questioned, but the consistency between all four cohorts strengthens the association. The death rate from carcinoma in other sites is also somewhat greater than expected, but there is not the same consistency from one cohort to another. It will be seen that the death rates from pulmonary carcinoma greatly exceed those from pleural and peritoneal mesothelioma combined in all cohorts, and exceed those from asbestosis in at least three cohorts. As may be expected, the death rate from causes other than cancer and asbestosis is less than that of the general population in three of the cohorts ("healthy worker effect"); it is difficult to explain why this should not be so in the amosite factory workers.

TABLE 12–1

Comparative Mortality Rates in Cohorts of Asbestos Workers

Cause of death	Cohort 1[a] 623 New York–New Jersey insulators			Cohort 2[a] 17,800 United States–Canada insulators			Cohort 3 933 amosite factory workers			Cohort 4 689 asbestos factory workers			All cohorts[b]		
	Obs	Exp.[c]	Ratios	Obs	Exp.[c]	Ratios	Obs	Exp.[c]	Ratios	Obs	Exp.[c]	Ratios	Obs	Exp.[c]	Ratios
Rates for different categories of cause of death															
All causes	444	300.7	1.48	1358	960.0	1.41	524	319.5	1.64	199	134.3	1.48	2525	1714.5	1.47
Cancer, all sites	198	51.3	3.86	575	175.6	3.23	163	54.6	2.99	72	27.8	2.59	1008	309.3	3.26
Pulmonary carcinoma	89	11.7	7.62	275	55.9	4.92	84	13.4	6.29	27	8.4	3.21	475	89.4	5.31
Pleural mesothelioma	10	—	—	29	—	—	5	—	—	8	—	—	52	—	—
Peritoneal mesoth	25	—	—	63	—	—	6	—	—	7	—	—	101	—	—
GI cancer	40	12.6	3.17	61	37.8	1.61	26	12.5	2.09	13	5.0	2.60	140	67.9	2.06
Other cancer	34	27.0	1.26	147	81.9	1.80	42	28.7	1.46	17	14.4	1.18	240	152.0	1.58
Asbestosis	37	—	—	101	—	—	27	—	—	24	—	—	189	—	—
All other causes	209	249.4	0.84	682	784.5	0.87	334	—	—	103	106.5	0.97	1328	—	—
Prevalence ratios for different causes															
Pulmon. carcin. mesoth.		2.54			2.99			7.64			1.80			2.91	
Pulmon. carcin. GI carcin.		2.23			4.51			3.23			2.08			3.39	
Pulmon. carcin. asbestosis		2.41			2.72			3.11			1.13			2.51	
Mesoth. asbestosis		0.96			0.91			0.41			0.63			0.86	

[a] 280 men of Cohort 1 are included in Cohort 2 so that the results are not entirely independent.
[b] Expected on the basis of age-specific death rates for the United States provided by the National Office of Vital Statistics

The experience reported by Newhouse for the workers in an East London asbestos factory, 1931–1970, closely matches that of the Mount Sinai cohorts (544). Table 12–2 gives the mortality data for workers with different degrees of exposure. [A]

Kogan *et al.* give the mortality ratios shown in Table 12–3 for asbestos miners and millers in the Urals, 1948–1967 (414). The age distribution given for the ratios is rather peculiar: much higher in the 30–39 and over-50 year brackets for men, and very much higher in the over-50 year bracket for women. In the absence of absolute numbers it is difficult to evaluate these irregularities, but the raised ratios for the workers as a whole are consistent with United States and British experience.

TABLE 12–2

Comparative Mortality of London Asbestos Workers, 1931–1970 (544)[a]

Cause of death	Exposure: Low-Mod <2 yr, 1861 men		Low-Mod >2 yr, 1178 men		Severe <2 yr, 2417 men		Severe >2 yr, 1304 men		Severe <2 yr, 557 women		Severe >2 yr, 239 women	
	Obs.	Exp.[b]	Obs.	Exp.	Obs.	Exp.	Obs.	Exp.	Obs.	Exp.	Obs.	Exp.
All causes	70	74.8	61	54.9	105	67.4	114	70.8	55	49.9	56	24.5
Cancer of lung and pleura	6	6.1	10	4.8	20	6.6	36	6.4	6	1.0	14	0.5
Other cancers	12	10.0	12	7.4	19	9.6	23	9.8	16	12.4	17	6.1
Mesothelioma	2	—	5	—	8	—	9	—	6	—	5	—

[a] With kind permission of M. L. Newhouse and the publishers of the *Annals of Occupational Hygiene*.

[b] Expected number based on similar population of England and Wales.

TABLE 12–3

Mortality Ratios for Asbestos Miners and Millers in the Urals, 1948–1967 (414)

Cause of death	Men: Mining	Men: Beneficiation	Women: Mining	Women: Beneficiation
Lung cancer	2.0	2.1	2.1	1.4
Stomach cancer	1.2	1.5	0.8	1.2
Intestinal cancer	1.5	—	0.8	0.9
Cancer of uterus	—	—	0.6	1.7
Cancer of other sites	1.8	1.7	0.5	1.3
All malignant tumors	1.6	1.6	0.8	1.3

That Japan is probably having similar experience is indicated by data published by Sera and colleagues for the Sennan district of Osaka Prefecture (386). Among 1,100 workers there using chrysotile from Quebec, 40 cases of asbestosis were admitted to hospital and 10 had carcinoma of the lung (25%). This incidence compares with 13 lung cancers among 279 (4.3%) with silicosis and 5 in 53 (9.4%) with other pneumoconioses.

Stell and McGill found that 31 out of 100 patients in Liverpool with squamous carcinoma of the larynx had experienced an important degree of asbestos exposure, as compared with only 3 out of 100 control patients (714). However, they were heavier cigarette smokers as a group. More recently, Shettigara and Morgan reported a highly significant association between asbestos exposure and laryngeal cancer, and a less strong association with cigarette smoking, in 43 matched pairs of cases (678). Gerber reported five tumors of the hemopoietic system in 35 autopsies on persons with asbestosis (266), but this is not in accord with our experience.

Dose–Response Relationships (Second Criterion)

The data just reviewed certainly establish a strong prima facie case for an increased risk of carcinoma, and particularly of pulmonary carcinoma, in persons exposed to asbestos, but it is well to follow through using the other criteria to pinpoint the etiological relationship a little more precisely. From what has been said in previous chapters about time and intensity factors that affect the appearance of asbestos disease, and from our general knowledge of carcinogenesis, we would expect intensity of dose, duration of exposure, and lapse of time since initial exposure to affect the appearance of tumors. Inasmuch as asbestos is only one of the factors that enter into the production of carcinoma, it will be more appropriate in further discussion to use these headings rather than those employed for mesothelioma.

Relation of Disease to Intensity of Exposure

In the data quoted above from Newhouse, the mortality ratio (the number of times by which the observed deaths exceed the expected) is two to three times higher in those men experiencing "severe" exposure than in those with only "low-moderate" exposure. However, this relationship was not found for lung carcinoma in a cohort of 689 asbestos product factors and textile workers studied at Mount Sinai over the period 1959–1971, in sharp distinction from the close relationship found for deaths from asbestosis (Table 12–4). This could be a matter of

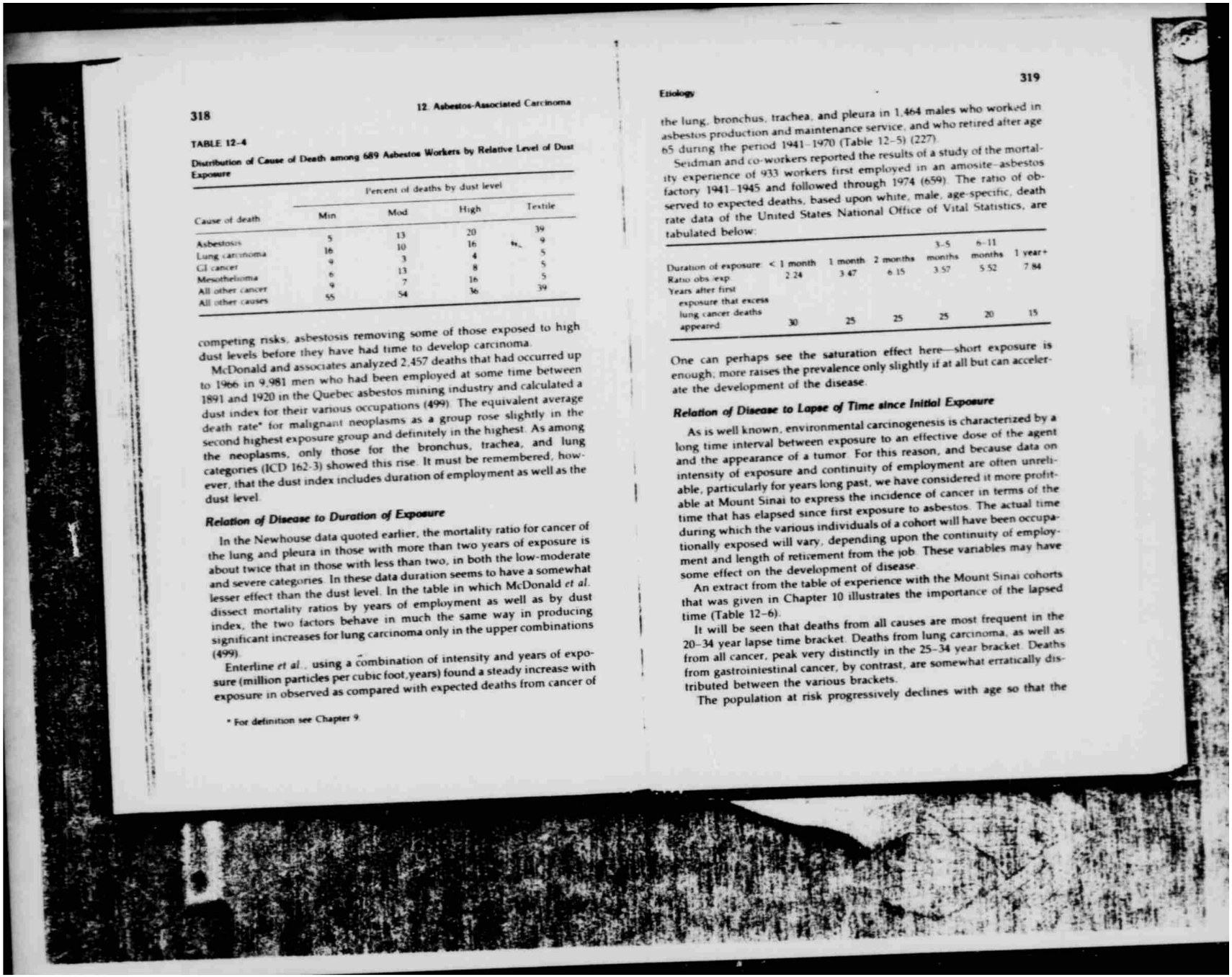


TABLE 12-4

Distribution of Cause of Death among 689 Asbestos Workers by Relative Level of Dust Exposure

Cause of death	Percent of deaths by dust level			
	Min	Mod	High	Textile
Asbestosis	5	13	20	39
Lung carcinoma	16	10	16	9
GI cancer	9	3	4	5
Mesothelioma	6	13	8	5
All other cancer	9	7	16	5
All other causes	55	54	36	39

competing risks, asbestosis removing some of those exposed to high dust levels before they have had time to develop carcinoma.

McDonald and associates analyzed 2,457 deaths that had occurred up to 1966 in 9,981 men who had been employed at some time between 1891 and 1920 in the Quebec asbestos mining industry and calculated a dust index for their various occupations (499). The equivalent average death rate* for malignant neoplasms as a group rose slightly in the second highest exposure group and definitely in the highest. As among the neoplasms, only those for the bronchus, trachea, and lung categories (ICD 162-3) showed this rise. It must be remembered, however, that the dust index includes duration of employment as well as the dust level.

Relation of Disease to Duration of Exposure

In the Newhouse data quoted earlier, the mortality ratio for cancer of the lung and pleura in those with more than two years of exposure is about twice that in those with less than two, in both the low-moderate and severe categories. In these data duration seems to have a somewhat lesser effect than the dust level. In the table in which McDonald *et al.* dissect mortality ratios by years of employment as well as by dust index, the two factors behave in much the same way in producing significant increases for lung carcinoma only in the upper combinations (499).

Enterline *et al.*, using a combination of intensity and years of exposure (million particles per cubic foot,years) found a steady increase with exposure in observed as compared with expected deaths from cancer of

* For definition see Chapter 9.

the lung, bronchus, trachea, and pleura in 1,464 males who worked in asbestos production and maintenance service, and who retired after age 65 during the period 1941–1970 (Table 12–5) (227).

Seidman and co-workers reported the results of a study of the mortality experience of 933 workers first employed in an amosite–asbestos factory 1941–1945 and followed through 1974 (659). The ratio of observed to expected deaths, based upon white, male, age-specific, death rate data of the United States National Office of Vital Statistics, are tabulated below:

Duration of exposure:	< 1 month	1 month	2 months	3–5 months	6–11 months	1 year+
Ratio obs/exp	2.24	3.47	6.15	3.57	5.52	7.84
Years after first exposure that excess lung cancer deaths appeared:	30	25	25	25	20	15

One can perhaps see the saturation effect here—short exposure is enough; more raises the prevalence only slightly if at all but can accelerate the development of the disease.

Relation of Disease to Lapse of Time since Initial Exposure

As is well known, environmental carcinogenesis is characterized by a long time interval between exposure to an effective dose of the agent and the appearance of a tumor. For this reason, and because data on intensity of exposure and continuity of employment are often unreliable, particularly for years long past, we have considered it more profitable at Mount Sinai to express the incidence of cancer in terms of the time that has elapsed since first exposure to asbestos. The actual time during which the various individuals of a cohort will have been occupationally exposed will vary, depending upon the continuity of employment and length of retirement from the job. These variables may have some effect on the development of disease.

An extract from the table of experience with the Mount Sinai cohorts that was given in Chapter 10 illustrates the importance of the lapsed time (Table 12–6).

It will be seen that deaths from all causes are most frequent in the 20–34 year lapse time bracket. Deaths from lung carcinoma, as well as from all cancer, peak very distinctly in the 25–34 year bracket. Deaths from gastrointestinal cancer, by contrast, are somewhat erratically distributed between the various brackets.

The population at risk progressively declines with age so that the

TABLE 12–5

Causes of Death in Retired Asbestos Workers in Relation to Cumulative Dust Exposure (227)[a]

Cause of death	Cumulative asbestos dust exposure (mppcf-yrs)															
	Under 125			125–249			250–499			500–749			over 750			
	Obs.	Exp.[b]	SMR[c]	Obs.	Exp.	SMR	Obs.	Exp.	SMR	Obs.	Exp.	SMR	Obs.	Exp.	SMR
All causes	365	345	106	162	140	116	184	157	117[d]	77	50	153[d]	34	26	130
Cancer of digestive system	27	22	123	5	9	56	19	10	190[d]	6	3	182	2	2	118
Cancer of lung, bronchus, trachea, and pleura	18	11	168	11	5	224[d]	16	5	296[d]	9	2	500[d]	5	1	556
All other cancer	29	24	122	?	10	71	17	11	154	3	4	83	2	2	105

[a] With the kind permission of P. Enterline and the publishers of the *Journal of Occupational Medicine*

[b] Expected deaths rounded to whole numbers

[c] SMR, Standardized Mortality Ratio as compared with entire United States white male population at same ages and time periods

[d] Significant at 5% level

TABLE 12–6

Deaths in Four Cohorts of Asbestos Workers in Relation to Lapse of Time since Initial Exposure[a]

Cause of death	Number of deaths by years since initial exposure							
	15–19	20–24	25–29	30–34	35–39	40–44	45–49	50+
All causes	220	291	324	269	189	201	173	172
Lung carcinoma	37	46	75	70	43	39	29	20
GI cancer	10	21	13	15	10	23	13	12
All cancer	73	106	133	141	83	100	71	57

[a] 250 men of Cohort 1 are included in Cohort 2 so that the results are not entirely independent.

deaths in the later years have greater significance than appears at first sight. Figure 10–6 set out the death rates in terms of the man-years since initial exposure of the population at risk in each bracket, on a semilogarithmic grid to permit comparison of rates based on different absolute numbers. Some irregularities are produced by the small number of individuals remaining in the upper two brackets, and by the small numbers of individuals developing gastrointestinal cancer.

The conclusions drawn from the graph in Chapter 10 may be repeated here: (a) lung cancer is responsible for more deaths to date in these workers than either asbestosis or mesothelioma and (b) that the distributions of death rates from mesothelioma and lung cancer, in relation to the lapse of time since initial exposure, follow the same slopes as does that from asbestosis in the lower exposure brackets, but falls off, more markedly with lung cancer than with mesothelioma, in the upper brackets of exposure. This last observation could mean that individuals with lung cancer, and to a lesser extent those with mesothelioma, are selected out by death after shorter periods of exposure, whereas sufficient numbers of those with asbestosis (i.e., the more moderate asbestosis of recent years) continue exposure into the longer periods before dying from that disease (see also Fig. 10–7).

Dose–Response Relationship for Gastrointestinal Cancer

Schneiderman statistically combined the meager data of McDonald on miners and of Enterline on retired industrial workers and found some evidence of a dose–response relationship as indicated in Fig. 12–1 (652). In the literature that he reviewed he found "only one paper [that] did not support the conclusion that increased exposure to inhaled asbestos particles leads to increased digestive system cancer." It would

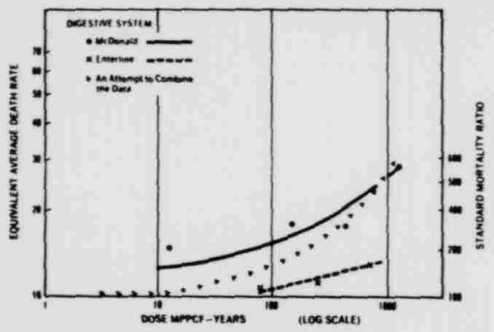


Fig. 12-1. Dose versus death rate from digestive system cancer reported by two investigators (652).

be wise, however, to reserve judgment until more extensive and more compatible data are available.

Concentration of Agent in Tissues (Third Criterion)

In 1959 Jacob and Bohlig examined the rate of occurrence of fatal lung cancer per 10,000 living individuals per year and found that it came to 82 for persons with severe asbestosis, 45 for those with moderate asbestosis, 11 for those with minimal asbestosis, and 3.7 for asbestos workers otherwise categorized (374). This favored a definite relationship between the liability of lung cancer and the degree of asbestosis which in turn is related to the concentration of fibers in the lungs. Konig, however, was of the opinion that the risk of pulmonary carcinoma did not increase with the severity of asbestosis (417). This left open the question of risk in persons who had not developed significant pulmonary fibrosis.

Harington, in summarizing today's position (310) remarked:". . . in persons with asbestosis, the death rate for cancer at this one site exceeds that for cancer at all sites in those not exposed to asbestos. . . . In general, it seems at the present time that in British asbestos workers there has been no excess of bronchogenic cancer in the absence of asbestosis." This last statement apparently refers to Davies' 1967 memorandum (170). Harington goes on to say, however, "In the United

States, an excess mortality from bronchogenic carcinoma may exist in the comparative absence of asbestosis in certain groups of workers exposed to asbestos. . . . In South Africa, bronchogenic carcinoma seems to occur in all South African asbestos areas and the percentage of cases is similar to those exposed to Cape crocidolite and amosite." [A]

In view of these divergent opinions about the existence of an increased risk of lung carcinoma in persons who have been exposed to asbestos, but have not developed radiological evidence of fibrosis, it is surprising that more attention has not been given to checking the concentration of asbestos bodies or fibers, or the pathological evidence of fibrosis, in the lungs of exposed persons who die with pulmonary carcinoma. The limited evidence so far reported is equivocal. Several authors have reported that the concentration of asbestos bodies in persons dying from lung cancer, randomly selected from the records of a general hospital, is not significantly altered from that in persons dying from other causes (20,218). But since the proportion of persons in a hospital population who are occupationally exposed to asbestos is small, even in a city with shipyards, the chance of finding a significant difference is not great. Bignon *et al.*, using concentration methods, however, did find a higher concentration of asbestos bodies in the lungs of 12 persons dying from primary lung cancer from among 100 autopsies on persons with respiratory disease in France (79). Warnock and Churg also found increased concentrations of asbestos bodies in consecutive cases of lung cancer as compared with other cases (775). As far back as 1938, Nordmann reported finding asbestos bodies and fibers in the substance of two lung cancers associated with asbestos but not in the metastases (552). Gold, using KOH extraction techniques, found variably raised counts of asbestos fibers in the lungs of persons dying from bronchial carcinoma and also in the tumors (284). Clearly, the relationship of fiber and asbestos body counts in the lungs and in the tumors to the occurrence of lung carcinoma in persons exposed to asbestos in whom pulmonary fibrosis has not been demonstrated is something that should be pursued with modern methods of detection, and some standardized indication should be given of the basis—radiological, macropathological, histological—used in making the diagnosis of "asbestosis."

Animal Experimentation (Fourth Criterion)

Early experimentation by Nordmann and Sorge produced some tumors, but the conditions of the experiment make interpretation of the results difficult (553). Gross *et al.* subjected 131 rats to finely milled chrysotile in very heavy air concentrations (42–146, with an average of

86 mg/m³) for six hours a day, five days a week, up to 62 weeks (299). Of the 72 animals surviving 16 or more months, 25 had lung tumors. Fifteen of these had received intratracheal injection of lye to impede lung clearance. The incidence in these impeded animals was about twice that in those not so treated. The malignant tumors were of wide variety: adenocarcinomas, fibrosarcomas, and squamous cell cancers, as well as a mesothelioma and a mucinous adenocarcinoma. It is difficult to project from these results to quantitative considerations for man. It should be noted, however, that intratracheal installation of test materials has rather more relevance to the development of bronchogenic carcinoma in man than it has to the induction of mesothelioma (640). Until recently, other investigators had not been successful, as had Saffiotti and coworkers, in producing pulmonary carcinoma through the inhalation of asbestos unless another carcinogen was simultaneously administered, such as benzo[a]pyrene (BAP) or acetylaminofluorene (310,698,732).

By contrast, the animal experiments recently reported by Wagner and his associates, which stand as a model of experimental approach, produced unequivocal evidence of the carcinogenicity of asbestos at least for rat lung, and strongly support the conclusions suggested by the epidemiological evidence so far reviewed insofar as lung tumors are concerned (773). Because of their importance some of the details will be given.

SPF Wistar rats were exposed by inhalation to dust clouds of the UICC standard reference samples for different periods of one day to two years. The mean respirable dust concentrations varied from 9.7–14.1 mg/m³ in the animals exposed for only one day, but through daily adjustment of the cumulative dosage the variability was reduced for the longer experiments to a range of 10.1–12.6 mg/m³. Measurements of the weight of dust in the lungs showed a steadily increasing accumulation of amphiboles with continued exposure, reaching 16.8 mg of amosite after 24 months. But the accumulation of the chrysotiles was much less, with a maximum of 1.4 mg after 12 months with the Rhodesian variety.

The number of animals with lung tumors is given in Table 12-7, and the number of tumors developing at other sites in Table 12-8, both taken from the cited report. The inhalation of asbestos by these animals did not bring about an increase in the incidence of either benign or malignant tumors in organs other than the lungs. [A]

Other Influential Factors (Fifth Criterion)

Now that cigarette smoking has been established as a major cause of bronchogenic carcinoma in man, the effect of this habit on the incidence in persons exposed to asbestos is clearly one to be explored. (It is

TABLE 12-7

Number of Rats Developing Lung Tumor after Inhalation of Asbestos (773)[a]

Exposure	No. of rats at risk[b]	No. with lung tumor	Type of lung tumor: Adenoma	Adenomatosis	Adenocarcinoma	Squamous carcinoma	No. with mesothelioma
Amosite							
1 day	45	3	3	0	0	0	1
3 months	37	10	7	3	0	0	0
6 months	18	2	1	0	1	0	0
12 months	25	10	5	4	1	0	0
24 months	21	13	3	1	3	6	0
	146	38	19	8	5	6	1
Anthophyllite							
1 day	44	2	2	0	0	0	0
3 months	37	6	6	0	0	0	0
6 months	18	6	3	1	1	1	0
12 months	28	20	9	6	4(1)	1	1
24 months	18	16	2	5	3	6	1
	145	50	22	12	8(1)	8	2
Crocidolite							
1 day	43	6	5	0	1	0	1
3 months	38	14	10	2	1	1(1)	1
6 months	18	4	2	2	0	0	0
12 months	26	18	5	4	3	6	2
24 months	18	13	4	5	2(1)	2(1)	0
	141	55	26	13	7(1)	9(2)	4
Chrysotile (Canadian)							
1 day	42	1	0	0	1(1)	0	0
3 months	34	18	15	0	3	0	0
6 months	17	5	2	2	0	1	0
12 months	23	11	1	3	6(1)	1(1)	3
24 months	21	10	2	3	1(1)	4(2)	4
	137	45	20	8	11(3)	6(3)	4
Chrysotile (Rhodesian)							
1 day	45	5	4	0	1	0	0
3 months	36	16	11	2	3(1)	0	0
6 months	19	8	2	3	3(1)	0	0
12 months	27	19	2	4	7(2)	6(4)	0
24 months	17	11	0	1	5(2)	5	0
	144	59	19	10	19(6)	11(4)	0

TABLE 12-7 Continued

Exposure	No. of rats at risk[a]	No. with lung tumor	Type of lung tumor: Adenoma	Adenomatosis	Adenocarcinoma[b]	Squamous carcinoma	No. with mesothelioma
Control							
1 day	44	4	4	0	0	0	0
3 months	40	3	3	0	0	0	0
6–24 months	42	0	0	0	0	0	0
	126	7	7	0	0	0	0

[a] With the kind permission of J. C. Wagner and the publishers of the *British Journal of Cancer*.
[b] Rats which survived at least 300 days after start of exposure.
[c] Numbers in parentheses are those with metastases.

TABLE 12-8

Number of Tumors at Sites Other Than Lung Developing in Rats after Inhalation of Asbestos (773)[a]

Type of fiber	Benign: Breast	Pituitary	Other	Malignant
Amosite	22	40	4	8
Anthophyllite	16	38	4	15
Crocidolite	20	31	4	10
Canadian chrysotile	23	26	7	7
Rhodesian chrysotile	19	37	9	3
Controls	20	34	2	13

[a] With kind permission of J. C. Wagner and the publishers of the *British Journal of Cancer*.

surprising that more has not been done to introduce this factor into animal experiments with asbestos; perhaps the cost of running sufficient numbers of dogs for a sufficiently long period of time is a deterrent.)

The preliminary data of Table 12–9 on the effect of cigarette smoking have been obtained on two cohorts followed by the Mount Sinai investigators. It will be seen that those asbestos workers who do not smoke enjoy a lower death rate than the average population of white males in the United States, many of whom smoke. This advantage does not extend, however, to all forms of cancer. It would seem that something about asbestos exposure increases the overall risk of cancer even in

TABLE 12-9

Effect of Cigarette Smoking on Development of Pulmonary Carcinoma in Asbestos Insulation Workers (Preliminary data)

Cohort	No history of cigarette smoking: Exp.[a]	Obs.	Ratio	History of cigarette smoking: Exp.[a]	Obs.	Ratio
	370 New York–New Jersey insulation workers					
	87 men			283 men		
All cancer deaths	4.75	15	3.16	10.99	79	7.19
Lung cancer deaths	1.26	1	0.79	3.31	41	12.39
	17,800 United States–Canada asbestos insulation workers					
	2066 men			9590 men		
All cancer deaths	19.92	33	1.66	79.58	265	3.33
Lung cancer deaths	5.98	2	0.33	25.09	134	5.34
	Combined cohorts					
	2153 men			9873 men		
All cancer deaths	24.67	48	1.95	90.57	344	3.80
Lung cancer deaths	7.24	3	0.41	28.40	175	6.16

[a] Based on age specific lung cancer death rates for white males in the United States, disregarding smoking.

those who do not smoke; compared to smokers non-smoking asbestos workers have a decided advantage in avoiding lung cancer, but not other types of cancer. Those asbestos workers who do smoke cigarettes have a much greater risk of acquiring lung cancer than those who do not, and perhaps a somewhat greater risk of developing cancer in other sites. [A]

It is clear from the literature that *all types of asbestos fibers*, except perhaps crocidolite, have been incriminated in the production of pulmonary carcinoma (Table 12–10) (670). Wright has indicated that he would expect all types to be carcinogenic (804); the absence of reports of a carcinogenic effect of crocidolite might simply be a matter of its not being reported. Webster, in fact, finds the percentage of cases of bronchogenic carcinoma similar in those exposed to Cape crocidolite and amosite and high in those exposed to Transvaal crocidolite and chrysotile (781). There have been suggestions that the high incidence of

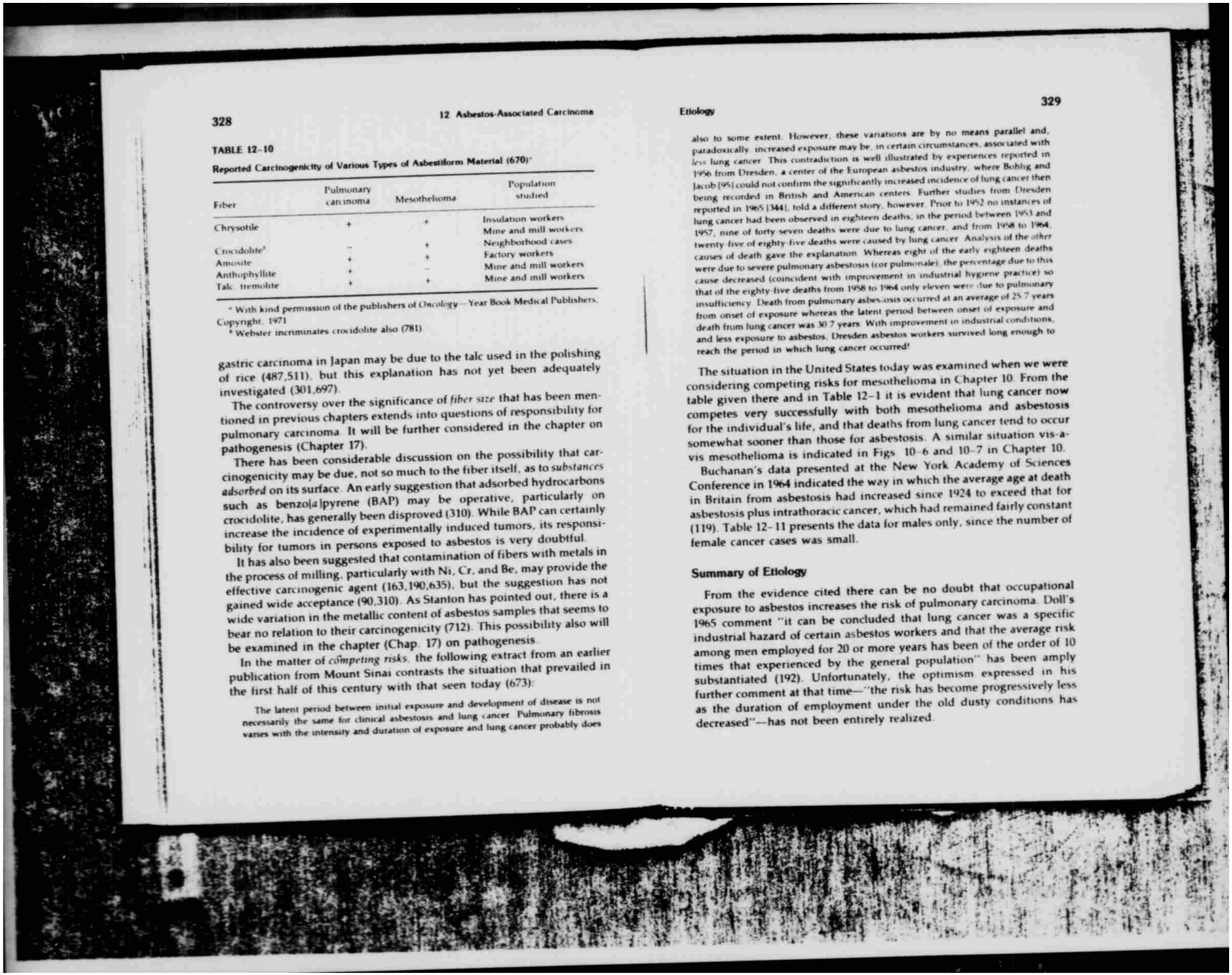


TABLE 12–10

Reported Carcinogenicity of Various Types of Asbestiform Material (670)[a]

Fiber	Pulmonary carcinoma	Mesothelioma	Population studied
Chrysotile	+	+	Insulation workers Mine and mill workers
Crocidolite[b]	–	+	Neighborhood cases
Amosite	+	+	Factory workers
Anthophyllite	+	–	Mine and mill workers
Talc, tremolite	+	+	Mine and mill workers

[a] With kind permission of the publishers of *Oncology*—Year Book Medical Publishers, Copyright, 1971

[b] Webster incriminates crocidolite also (781)

gastric carcinoma in Japan may be due to the talc used in the polishing of rice (487,511), but this explanation has not yet been adequately investigated (301,697).

The controversy over the significance of *fiber size* that has been mentioned in previous chapters extends into questions of responsibility for pulmonary carcinoma. It will be further considered in the chapter on pathogenesis (Chapter 17).

There has been considerable discussion on the possibility that carcinogenicity may be due, not so much to the fiber itself, as to *substances adsorbed* on its surface. An early suggestion that adsorbed hydrocarbons such as benzo[*a*]pyrene (BAP) may be operative, particularly on crocidolite, has generally been disproved (310). While BAP can certainly increase the incidence of experimentally induced tumors, its responsibility for tumors in persons exposed to asbestos is very doubtful.

It has also been suggested that contamination of fibers with metals in the process of milling, particularly with Ni, Cr, and Be, may provide the effective carcinogenic agent (163,190,635), but the suggestion has not gained wide acceptance (90,310). As Stanton has pointed out, there is a wide variation in the metallic content of asbestos samples that seems to bear no relation to their carcinogenicity (712). This possibility also will be examined in the chapter (Chap. 17) on pathogenesis.

In the matter of *competing risks*, the following extract from an earlier publication from Mount Sinai contrasts the situation that prevailed in the first half of this century with that seen today (673):

> The latent period between initial exposure and development of disease is not necessarily the same for clinical asbestosis and lung cancer. Pulmonary fibrosis varies with the intensity and duration of exposure and lung cancer probably does

> also to some extent. However, these variations are by no means parallel and, paradoxically, increased exposure may be, in certain circumstances, associated with *less* lung cancer. This contradiction is well illustrated by experiences reported in 1956 from Dresden, a center of the European asbestos industry, where Bohlig and Jacob [95] could not confirm the significantly increased incidence of lung cancer then being recorded in British and American centers. Further studies from Dresden reported in 1965 [344], told a different story, however. Prior to 1952 no instances of lung cancer had been observed in eighteen deaths, in the period between 1953 and 1957, nine of forty-seven deaths were due to lung cancer, and from 1958 to 1964, twenty-five of eighty-five deaths were caused by lung cancer. Analysis of the *other* causes of death gave the explanation. Whereas eight of the early eighteen deaths were due to severe pulmonary asbestosis (cor pulmonale), the percentage due to this cause decreased (coincident with improvement in industrial hygiene practice) so that of the eighty-five deaths from 1958 to 1964 only eleven were due to pulmonary insufficiency. Death from pulmonary asbestosis occurred at an average of 25.7 years from onset of exposure whereas the latent period between onset of exposure and death from lung cancer was 30.7 years. With improvement in industrial conditions, and less exposure to asbestos, Dresden asbestos workers survived long enough to reach the period in which lung cancer occurred!

The situation in the United States today was examined when we were considering competing risks for mesothelioma in Chapter 10. From the table given there and in Table 12–1 it is evident that lung cancer now competes very successfully with both mesothelioma and asbestosis for the individual's life, and that deaths from lung cancer tend to occur somewhat sooner than those for asbestosis. A similar situation vis-a-vis mesothelioma is indicated in Figs. 10–6 and 10–7 in Chapter 10.

Buchanan's data presented at the New York Academy of Sciences Conference in 1964 indicated the way in which the average age at death in Britain from asbestosis had increased since 1924 to exceed that for asbestosis plus intrathoracic cancer, which had remained fairly constant (119). Table 12–11 presents the data for males only, since the number of female cancer cases was small.

Summary of Etiology

From the evidence cited there can be no doubt that occupational exposure to asbestos increases the risk of pulmonary carcinoma. Doll's 1965 comment "it can be concluded that lung cancer was a specific industrial hazard of certain asbestos workers and that the average risk among men employed for 20 or more years has been of the order of 10 times that experienced by the general population" has been amply substantiated (192). Unfortunately, the optimism expressed in his further comment at that time—"the risk has become progressively less as the duration of employment under the old dusty conditions has decreased"—has not been entirely realized.

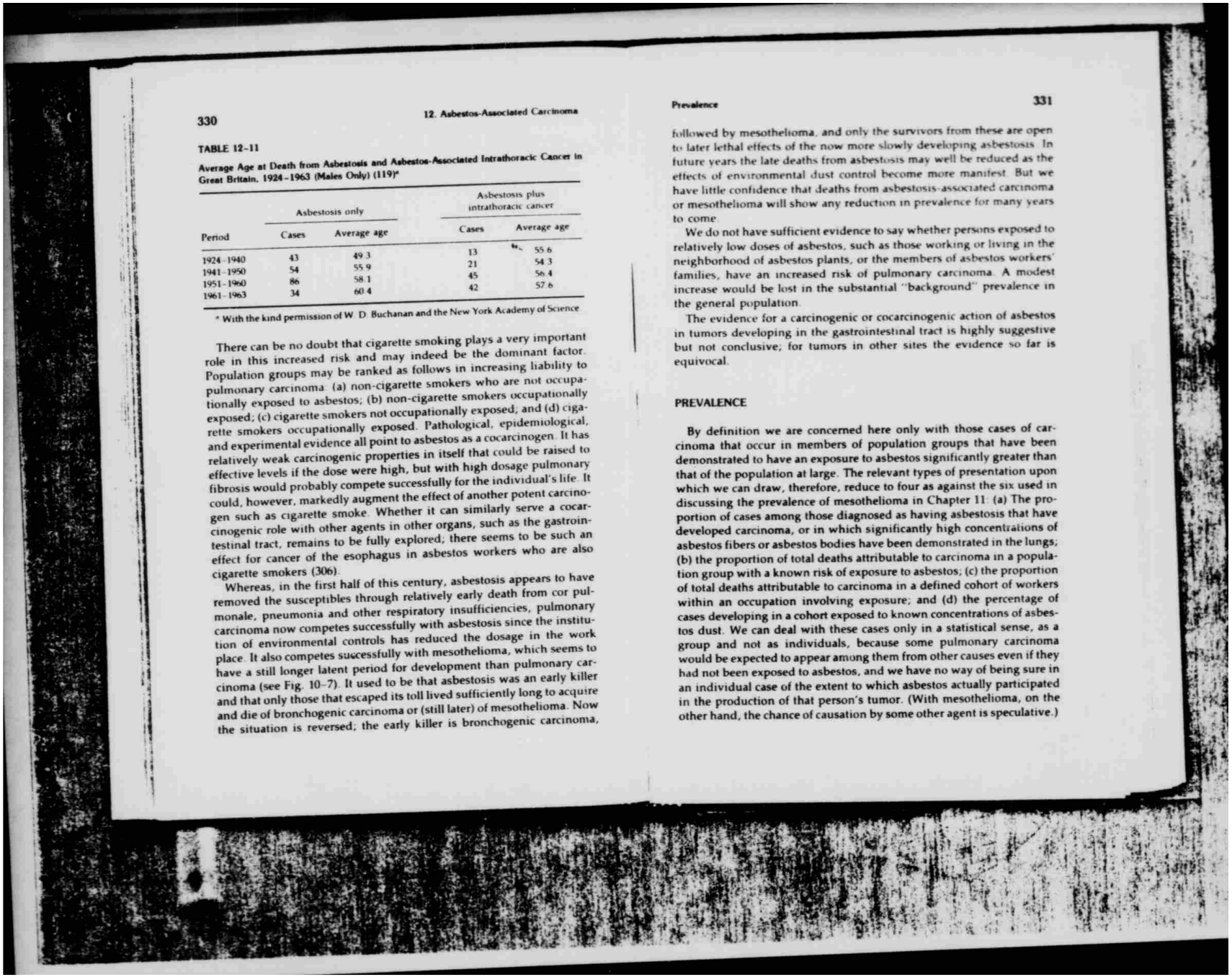


TABLE 12-11

Average Age at Death from Asbestosis and Asbestos-Associated Intrathoracic Cancer in Great Britain, 1924–1963 (Males Only) (119)[a]

Period	Asbestosis only		Asbestosis plus intrathoracic cancer	
	Cases	Average age	Cases	Average age
1924–1940	43	49.3	13	55.6
1941–1950	54	55.9	21	54.3
1951–1960	86	58.1	45	56.4
1961–1963	34	60.4	42	57.6

[a] With the kind permission of W. D. Buchanan and the New York Academy of Science

There can be no doubt that cigarette smoking plays a very important role in this increased risk and may indeed be the dominant factor. Population groups may be ranked as follows in increasing liability to pulmonary carcinoma: (a) non-cigarette smokers who are not occupationally exposed to asbestos; (b) non-cigarette smokers occupationally exposed; (c) cigarette smokers not occupationally exposed; and (d) cigarette smokers occupationally exposed. Pathological, epidemiological, and experimental evidence all point to asbestos as a cocarcinogen. It has relatively weak carcinogenic properties in itself that could be raised to effective levels if the dose were high, but with high dosage pulmonary fibrosis would probably compete successfully for the individual's life. It could, however, markedly augment the effect of another potent carcinogen such as cigarette smoke. Whether it can similarly serve a cocarcinogenic role with other agents in other organs, such as the gastrointestinal tract, remains to be fully explored; there seems to be such an effect for cancer of the esophagus in asbestos workers who are also cigarette smokers (306).

Whereas, in the first half of this century, asbestosis appears to have removed the susceptibles through relatively early death from cor pulmonale, pneumonia and other respiratory insufficiencies, pulmonary carcinoma now competes successfully with asbestosis since the institution of environmental controls has reduced the dosage in the work place. It also competes successfully with mesothelioma, which seems to have a still longer latent period for development than pulmonary carcinoma (see Fig. 10–7). It used to be that asbestosis was an early killer and that only those that escaped its toll lived sufficiently long to acquire and die of bronchogenic carcinoma or (still later) of mesothelioma. Now the situation is reversed; the early killer is bronchogenic carcinoma,

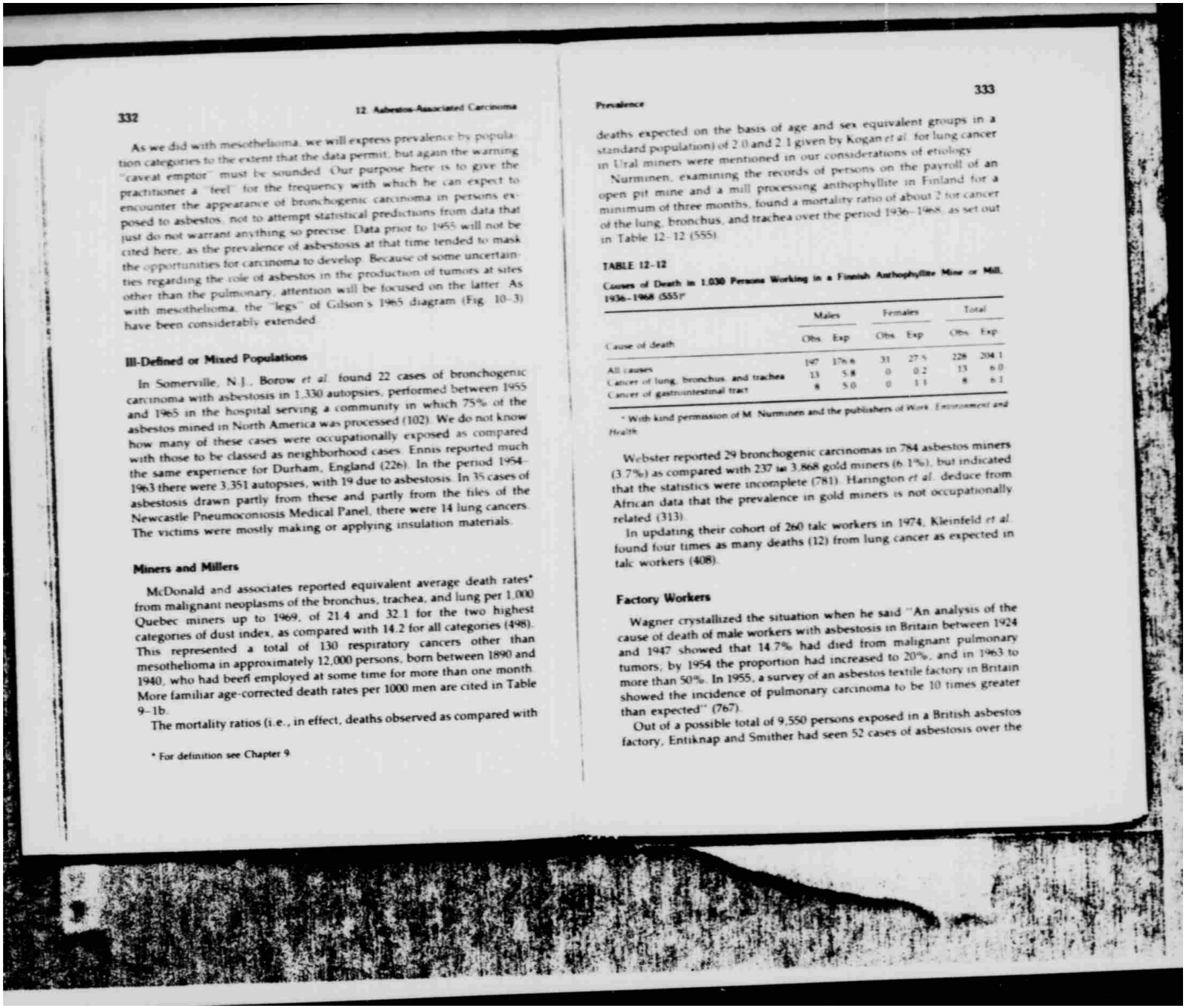
followed by mesothelioma, and only the survivors from these are open to later lethal effects of the now more slowly developing asbestosis. In future years the late deaths from asbestosis may well be reduced as the effects of environmental dust control become more manifest. But we have little confidence that deaths from asbestosis-associated carcinoma or mesothelioma will show any reduction in prevalence for many years to come.

We do not have sufficient evidence to say whether persons exposed to relatively low doses of asbestos, such as those working or living in the neighborhood of asbestos plants, or the members of asbestos workers' families, have an increased risk of pulmonary carcinoma. A modest increase would be lost in the substantial "background" prevalence in the general population.

The evidence for a carcinogenic or cocarcinogenic action of asbestos in tumors developing in the gastrointestinal tract is highly suggestive but not conclusive; for tumors in other sites the evidence so far is equivocal.

PREVALENCE

By definition we are concerned here only with those cases of carcinoma that occur in members of population groups that have been demonstrated to have an exposure to asbestos significantly greater than that of the population at large. The relevant types of presentation upon which we can draw, therefore, reduce to four as against the six used in discussing the prevalence of mesothelioma in Chapter 11: (a) The proportion of cases among those diagnosed as having asbestosis that have developed carcinoma, or in which significantly high concentrations of asbestos fibers or asbestos bodies have been demonstrated in the lungs; (b) the proportion of total deaths attributable to carcinoma in a population group with a known risk of exposure to asbestos; (c) the proportion of total deaths attributable to carcinoma in a defined cohort of workers within an occupation involving exposure; and (d) the percentage of cases developing in a cohort exposed to known concentrations of asbestos dust. We can deal with these cases only in a statistical sense, as a group and not as individuals, because some pulmonary carcinoma would be expected to appear among them from other causes even if they had not been exposed to asbestos, and we have no way of being sure in an individual case of the extent to which asbestos actually participated in the production of that person's tumor. (With mesothelioma, on the other hand, the chance of causation by some other agent is speculative.)



As we did with mesothelioma, we will express prevalence by population categories to the extent that the data permit, but again the warning "caveat emptor" must be sounded. Our purpose here is to give the practitioner a "feel" for the frequency with which he can expect to encounter the appearance of bronchogenic carcinoma in persons exposed to asbestos, not to attempt statistical predictions from data that just do not warrant anything so precise. Data prior to 1955 will not be cited here, as the prevalence of asbestosis at that time tended to mask the opportunities for carcinoma to develop. Because of some uncertainties regarding the role of asbestos in the production of tumors at sites other than the pulmonary, attention will be focused on the latter. As with mesothelioma, the "legs" of Gilson's 1965 diagram (Fig. 10–3) have been considerably extended.

Ill-Defined or Mixed Populations

In Somerville, N.J., Borow *et al.* found 22 cases of bronchogenic carcinoma with asbestosis in 1,330 autopsies, performed between 1955 and 1965 in the hospital serving a community in which 75% of the asbestos mined in North America was processed (102). We do not know how many of these cases were occupationally exposed as compared with those to be classed as neighborhood cases. Ennis reported much the same experience for Durham, England (226). In the period 1954–1963 there were 3,351 autopsies, with 19 due to asbestosis. In 35 cases of asbestosis drawn partly from these and partly from the files of the Newcastle Pneumoconiosis Medical Panel, there were 14 lung cancers. The victims were mostly making or applying insulation materials.

Miners and Millers

McDonald and associates reported equivalent average death rates* from malignant neoplasms of the bronchus, trachea, and lung per 1,000 Quebec miners up to 1969, of 21.4 and 32.1 for the two highest categories of dust index, as compared with 14.2 for all categories (498). This represented a total of 130 respiratory cancers other than mesothelioma in approximately 12,000 persons, born between 1890 and 1940, who had been employed at some time for more than one month. More familiar age-corrected death rates per 1000 men are cited in Table 9–1b.

The mortality ratios (i.e., in effect, deaths observed as compared with

* For definition see Chapter 9.

deaths expected on the basis of age and sex equivalent groups in a standard population) of 2.0 and 2.1 given by Kogan *et al.* for lung cancer in Ural miners were mentioned in our considerations of etiology.

Nurminen, examining the records of persons on the payroll of an open pit mine and a mill processing anthophyllite in Finland for a minimum of three months, found a mortality ratio of about 2 for cancer of the lung, bronchus, and trachea over the period 1936–1968, as set out in Table 12–12 (555).

TABLE 12-12

Causes of Death in 1,030 Persons Working in a Finnish Anthophyllite Mine or Mill, 1936–1968 (555)*

Cause of death	Males		Females		Total	
	Obs.	Exp.	Obs.	Exp.	Obs.	Exp.
All causes	197	176.6	31	27.5	228	204.1
Cancer of lung, bronchus, and trachea	13	5.8	0	0.2	13	6.0
Cancer of gastrointestinal tract	8	5.0	0	1.1	8	6.1

* With kind permission of M. Nurminen and the publishers of *Work, Environment and Health*.

Webster reported 29 bronchogenic carcinomas in 784 asbestos miners (3.7%) as compared with 237 in 3,868 gold miners (6.1%), but indicated that the statistics were incomplete (781). Harington *et al.* deduce from African data that the prevalence in gold miners is not occupationally related (313).

In updating their cohort of 260 talc workers in 1974, Kleinfeld *et al.* found four times as many deaths (12) from lung cancer as expected in talc workers (408).

Factory Workers

Wagner crystallized the situation when he said "An analysis of the cause of death of male workers with asbestosis in Britain between 1924 and 1947 showed that 14.7% had died from malignant pulmonary tumors; by 1954 the proportion had increased to 20%, and in 1963 to more than 50%. In 1955, a survey of an asbestos textile factory in Britain showed the incidence of pulmonary carcinoma to be 10 times greater than expected" (767).

Out of a possible total of 9,550 persons exposed in a British asbestos factory, Entiknap and Smither had seen 52 cases of asbestosis over the

period 1956–1962, in whom 19 (36%) had pulmonary carcinomas, none of which involved the pleura (230). We do not know how many of the employees who did not come to autopsy, and presumably did not have asbestosis, also had lung cancer. Some idea of the *relative proportions*, however, is given by Doll's earlier report of 18 cases of lung cancer in those employed at a large asbestos works from 1935–1953, 15 of which were accompanied by asbestosis and three not (192).

In an extension of Doll's 1955 study, Smither, Hill, and others reported in 1965 that of 198 men employed over 20 years at the end of 1961, deaths from all causes were 61 as compared with 28.40 expected, and included 20 from lung cancer as against 2.25 expected (700). The incidence was highest in those who had already been employed over 10 years in 1933, and the hope was implied that the incidence could be expected to decline in future years through the introduction of dust controls. The situation in 1974, as reported recently by Howard *et al.*, is that the ratios of observed to expected deaths from lung cancer are significantly high in males who have spent more than 20 years in areas of exposure risk: 9.5 in those employed 10 or more years before 1933, and 3.3 in those employed less than 10 years before 1933 (357).

As indicated earlier, Newhouse found the ratio of observed/expected deaths from pulmonary carcinoma to go from approximately one in male asbestos factory workers exposed to low-moderate concentrations for less than two years, to 5.63 in those with severe exposure for over two years, and to the extraordinary value of 27 in women with severe exposure for over two years.

Japanese experience was also quoted earlier of 10 pulmonary carcinomas out of 40 cases of asbestosis admitted to hospitals. Vigliani and associates reported in 1965 that they had found 15 lung carcinomas in 172 deaths (8.7%) of persons with asbestosis, as against 1.7% in persons with silicosis (759).

For the United States, Mancuso and Coulter reported that the greatest contribution to excess neoplastic deaths in a cohort of asbestos workers over the period 1940–mid-1960 was carcinoma of the lung, bronchus, and trachea: 15 as compared with 5.42 expected among males and 4 as against 0.19 expected in females (475). (Cigarette smoking was probably less common among women at that time than it is today.)

Kleinfeld *et al.* found that 10 out of 46 deaths in a cohort of 152 asbestos workers with more than 15 years of exposure by 1965 were due to pulmonary carcinoma, as compared with 1.43 expected (405).

Enterline and Kendrick, discussing deaths in white males who worked in selected United States asbestos and cotton textile mills at some time during 1948–1951, and were followed through 1963, reported

TABLE 12-13

Standardized Mortality Ratios for White Male Workers in United States Textile Mills, 1948–1963 (228)[a]

Cause of death	Asbestos building products	Asbestos friction material	Asbestos textile products	Cotton textile products
All deaths	88.5	88.8	120.6	88.2
All cancer	88.1	102.3	148.4	69.7
Cancer of respiratory system	130.4	123.7	228.6	31.1[b]
Cancer of digestive system	88.8	119.2	146.3	96.3

[a] With kind permission of P. E. Enterline and the publishers of *Archives of Environmental Health*.
[b] Number of deaths less than 10.

the standardized mortality ratios of Table 12–13 (228): other data reported by Enterline and colleagues on retired employees were given earlier.

In the table cited earlier for the Mount Sinai cohorts, the ratios of observed/expected deaths for pulmonary carcinoma were given as 6.29 for workers in an amosite factory and 3.21 for those in a chrysotile factory. The corresponding ratios for cancer of the gastrointestinal tract were 2.09 and 2.60, respectively.

Construction and Engineering Workers

Elmes, in following through 1968 170 men who were insulation workers in Belfast in 1940, found a standardized mortality ratio of 6.70 for all types of cancer and 17.60 for cancer of the larynx, lung, and pleura, but mesothelioma was almost certainly included in these data (219).

The experience at Mount Sinai with the cohorts of New York–New Jersey and United States–Canada insulation workers cited earlier gives ratios of observed/expected deaths from pulmonary carcinoma of 7.62 and 4.92, and for cancer of the gastrointestinal tract 3.17 and 1.61, respectively.

Summary of Prevalence

Many of the remarks that were made about the prevalence of mesothelioma in the preceding chapter (Chapter 11) could be applied with equal truth to the prevalence of asbestos-associated carcinoma, for example:

1. The available data are incomplete and not always reliable, but the weight of the evidence when considered in its totality is overwhelming—pulmonary carcinoma occurs from 2 to 8 times more frequently in persons exposed to asbestos than it does in a comparable population not so exposed.

2. The prevalence has increased over the last twenty years, partly as the result of exposed persons not dying at midlife from asbestosis with the same frequency as formerly.

But there are many features that apply to pulmonary carcinoma alone, such as the prevalence of pulmonary carcinoma in persons exposed to asbestos is three or more times that of mesothelioma, the development of pulmonary carcinoma in persons exposed to asbestos is very closely tied to their indulgence in cigarette smoking; in the absence of smoking, there may be an increase in the prevalence but it is not significant. The prevalence of pulmonary carcinoma in those exposed to asbestos and to smoking may be related to the degree of dust exposure, but the evidence is not strong.

It would seem that control of cigarette smoking would have a much greater impact on the incidence of bronchogenic cancer in asbestos workers than further reduction of dust levels (a very different situation than that which pertains with mesothelioma, in which smoking plays little if any role, and further dust control may be expected to reduce the incidence).

Part IV

Pathogenic Mechanisms

Principal Collaborators

J. CHURG
R. J. SCHNITZER
Y. SUZUKI
A. TEIRSTEIN

Published by AsbestosClaims.Law
asbestosclaims.law/library/25349/16