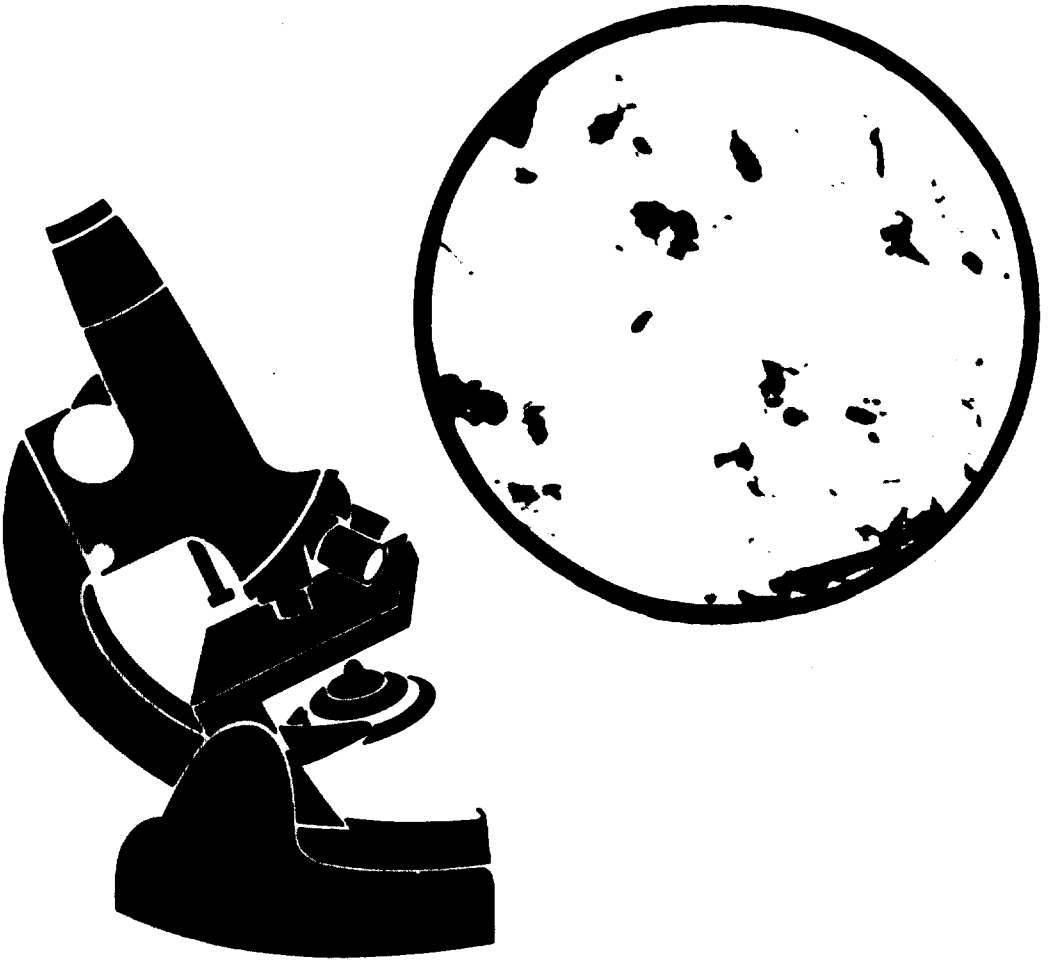
NIOSH

REVISED RECOMMENDED ASBESTOS STANDARD



U. S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
Public Health Service
Center for Disease Control
National Institute for Occupational Safety and Health

REVISED RECOMMENDED

ASBESTOS STANDARD

U. S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
Public Health Service
Center for Disease Control
National Institute for Occupational Safety and Health

DECEMBER 1976

For sale by the Superintendent of Documents, U.S. Government Printing Office, Washington, D.C. 20402

The Division of Surveillance, Hazard Evaluations, and Field Studies, National Institute for Occupational Safety and Health (NIOSH), having primary responsibility for development of a NIOSH position paper on health effects of occupational asbestos exposure, has critiqued all available data and prepared the following document for publication and transmittal to the Occupational Safety and Health Administration (OSHA), as requested by the Assistant Secretary of Labor. Primary responsibility for development of this document was shared by Richard A. Lemen and John M. Dement, with technical consultation provided by Dr. Joseph K. Wagoner. Individuals who served as the NIOSH review committee were:

Kenneth Bridbord, M.D.
David H. Groth, M.D.
Gerald J. Karches
James B. Lucas, M.D.
James H. Wills, Ph.D.

DHEW (NIOSH) Publication No. 77-169

REVISED RECOMMENDED
ASBESTOS STANDARD

Table of Contents

I. INTRODUCTION

When the asbestos criteria document was first published in 1972, the National Institute for Occupational Safety and Health (NIOSH) recommended a standard of 2.0 asbestos fibers/cubic centimeter (cc) of air based on a count of fibers greater than 5 micrometers (μm) in length. This standard was recommended with the stated belief that it would "prevent" asbestosis and with the open recognition that it would not "prevent" asbestos-induced neoplasms. Furthermore, data were presented which supported the fact that technology was available to achieve that standard and that the criteria would be subject to review and revision as necessary. Since the time that the asbestos criteria were published in 1972, sufficient additional data regarding asbestos-related disease have been developed to warrant reevaluation.

On June 7, 1972, the Occupational Safety and Health Administration (OSHA) promulgated a standard for occupational exposure to asbestos containing an 8-hour time-weighted average (TWA) concentration exposure limit of 5 fibers longer than 5 μm/cc of air, with a ceiling limitation against any exposure in excess of 10 such fibers/cc. The standard further provided that the 8-hour TWA was to be reduced to 2 fibers/cc on July 1, 1976.

As the result of a court case, OSHA decided that to achieve the most feasible occupational health protection, a reexamination of the standard's general premises and general structure was necessary. To this end, on October 9, 1975, OSHA announced a proposed rule-making to lower the exposure limit to an 8-hour TWA concentration of 0.5 asbestos fibers longer

than 5 μm/cc of air with a ceiling concentration of 5 fibers/cc of air determined by a sampling period of up to 15 minutes. On December 2, 1975, OSHA requested NIOSH to reevaluate the information available on the health effects of occupational exposure to asbestos fibers and to advise OSHA on the results of this study.

This document contains an updated review of the available information on the health effects of exposure to asbestos. In addition, NIOSH's proposal for a new numerical exposure limit is included.

Edward J. Baier

for John F. Finklea, M.D.
Director, National Institute for
Occupational Safety and Health

II. BIOLOGIC EFFECTS OF EXPOSURE ON ANIMALS

Carcinogenicity

The carcinogenicity of asbestos was studied through various routes of exposure

(a) Instillation

(1) Intratracheal Injection

This technique has been used to study co-carcinogenesis of chrysotile asbestos with benzo(a)pyrene in hamsters (Miller et al, 1965) and rats (Vosamae, 1972; Pylev, 1972; Pylev and Shabad, 1973; Shabad et al, 1974). In both species, it was demonstrated that the effect of chrysotile was additive to that of benzo(a)pyrene for tumors of the respiratory tract.

Shabad et al (1974) showed that intratracheal injection of 2 mg of Russian chrysotile on which 0.144 mg benzo(a)pyrene was absorbed (3 times at monthly intervals), or 2 mg of Russian chrysotile together with 5 mg benzo(a)pyrene (single injection) produced lung papillomas, epidermoid carcinomas, reticulosarcomas, or pleural mesotheliomas in 6/21 and 6/11 rats, respectively, within 9-28 months. No lung tumors or mesotheliomas occurred in 49 rats given 3 doses of 2 mg chrysotile alone or in 19 rats given a single dose of 5 mg benzo(a)pyrene alone during or up to 28 months of observation.

(2) Intraperitoneal (ip) Administration

Reeves et al (1971) gave ip injections of 0.3, 0.5, or 1.0 ml of a solution of 20 mg/ml amosite, crocidolite or chrysotile to groups of 11, 13, and 13 Charles River CD rats, respectively. Three peritoneal mesotheliomas were observed with chrysotile, three with crocidolite, and

none with amosite after 7-17 months. No data on control animals were reported.

Maltoni and Annoscia (1973) injected 25 mg of crocidolite into 50 male and 50 female Sprague-Dawley rats, 18 weeks old, and later observed 65 mesotheliomas-31 in males and 34 in females.

Pott and Friedrichs (1972) and Pott et al (1974) injected fibrous and granular dusts into the peritoneal cavities of Wistar rats. The dosage, number of inoculations, and results are shown in Tables II-1 and II-2.

After injection of powdered chrysotile, the latent period for the induction of tumors was found to be longer than that after injection of standard chrysotile. The rate of tumor occurrence was about 40% in both groups and was not distinctly influenced by the addition of benzo(a)pyrene. In another group, benzo(a)pyrene without asbestos induced tumors in 10% of the animals. Histologically, the types of tumors observed were connected with structures of the abdominal wall, including the serosa, and in isolated cases with those of the intestinal wall (Pott et al, 1972).

(3) Intrapleural Administration

All commercial types of asbestos have produced mesotheliomas in CD Wistar rats. A dose of 20 mg of the 5 UICC standard reference samples produced mesotheliomas in varying numbers - crocidolite, (61%); amosite, (36%); anthophyllite, (34%); Canadian chrysotile, (30%); Rhodesian chrysotile, (19%) (Wagner et al, 1974). The lowest dose used (0.5 mg chrysotile or crocidolite) produced mesotheliomas (Wagner et al, 1973). Stanton and Wrench (1972), using a dose of 40 mg asbestos dust on gelatin-coated fiber glass pledgets, found that three of the UICC samples,

crocidolite, amosite and Rhodesian chrysotile, all produced mesotheliomas in about 60% of the Osborne-Mendel rats. Pylev and Shabad (1973) induced mesotheliomas with 60 mg of Russian chrysotile. In all these studies there was a long latent period between inoculation and appearance of the tumors. Evidence that the response was dose-related was provided by Wagner et al (1973) and by Stanton (1973). Mesotheliomas have also been produced by other workers: in rats (Donna, 1970; Reeves et al, 1971), in hamsters (Smith et al, 1965) and in rabbits (Reeves et al, 1971). Groth et al (1975) reported no mesotheliomas or other neoplasms from chrysotile in 45 female discard-breeder albino rats, approximately 10 months old. However, all surviving tumor-free animals were killed at 90 or 150 days after injection--a time period insufficient for the development of mesotheliomas as demonstrated by the experiments of Wagner and Berry (1969).

The suggestion has been made that natural oils and waxes (Harrington, 1962) and contaminant oils from milling of the asbestos fiber (Harrington and Roe, 1965; Roe et al, 1966) or from plastic storage bags (Commins and Gibbs, 1969) contributed to the incidence of pleural tumors. However, samples from which the oils had been removed gave very similar results to untreated fiber (Wagner and Berry, 1969; Wagner et al, 1973).

Morgan and Holmes (1970) and Morgan et al (1971) showed that when asbestos was injected intrapleurally, the majority of the fibers were cleared from the lungs during the first 10 days; subsequently there was also a very slow elimination through the gut. In feeding experiments almost all of the fibers were eliminated. After intrapleural or subcutaneous inoculation, only a minute fraction of the finer fibers were translocated through the tissues. This finding was supported by the

studies of Kanazawa et al (1970).

The fiber diameter, length, and shape may be important in disease production. All of the eight separate sub-samples which were pooled in the UICC Canadian chrysotile reference sample (Timbrell and Rendall, 1972), when ground separately to a finer powder, produced a higher incidence of mesothelioma than the pooled sample. The highest incidence (66%) was produced by a separate superfine chrysotile sample (20 mg dose) fractionated from fine grade asbestos by water sedimentation (Wagner et al, 1973). Using UICC crocidolite, Stanton and Wrench (1972) found that partially pulverized material gave fewer mesotheliomas than did the standard unpulverized fiber. Prolonged fine grinding is known to destroy fiber and crystalline structure (Occella and Maddalon, 1963). Stanton (1973) showed that fibers of other materials, including glass, could induce mesotheliomas, but only when the diameter was of the same order as that of asbestos when measured by light microscopy.

In addition to the UICC standard reference samples, other fibers were injected intrapleurally into rats by Wagner et al (1973). Out of a group of 32 rats, mestheliomas occurred in 18 animals injected with a sample of brucite, 3 injected with a ceramic fiber, 1 each with barium sulphate, glass powder, and aluminum oxide. None occurred with a coarse glass fiber.

Wagner et al (1976) conducted a series of experiments comparing the biologic effects of a pure asbestos-free cosmetic talc with the superfine chrysotile asbestos used in previous experiments. In an intrapleural inoculation experiment, 48 rats were inoculated with each dust. Eighteen rats of the chrysotile group developed mesotheliomas, but

no tumors were seen in those given talc.

Further evidence on the importance of fiber diameter was provided by Wagner et al (1976), who reported on rats injected intrapleurally with glass fiber (Table II-3). Two samples of glass fiber were used, one with a median fiber diameter of 0.12 μm and the other with a median diameter of 1.8 μm. Four mesotheliomas were observed in 32 rats injected with the finer fiber and none with the coarser fiber. Also, the degree of mesothelial cell hyperplasia was more pronounced in the rats injected with the finer fiber. These results were comparable with those of the previous experiment.

Shabad et al (1974) reported that when 20 mg of Russian chrysotile was injected intrapleurally 3 times into 67 rats, 31 developed mesotheliomas within 2 years.

(b) Ingestion

Gross et al (1974) reported the results of a series of feeding experiments with chrysotile and crocidolite fed to rats of various origins. In groups of rats varying in number from 10 through 35, no significant differences in tumor incidence were observed in comparison with controls. Survival rates were not reported, sample sizes were small (from 10 through 35) and no pathologic details were given.

In another experiment, Wagner et al (1976) fed 100 mg/day of talc (5 days/week) or chrysotile in malted milk powder for 100 days over a 6-month period to groups of 32 Wistar SPF rats; 16 controls were fed only malted milk. The mean survival from the start of feeding was 614 days for talc, 618 for chrysotile, and 641 days for the controls. The only tumors which may have been associated with ingestion were two gastric leiomyosarcomas;

one in an animal fed talc and the other in one fed chrysotile. None occurred in the controls.

(c) Inhalation

Lynch et al (1957) exposed AC/Fl hybrid mice by inhalation to a commercial preparation of chrysotile asbestos and observed a higher incidence of multiple pulmonary adenomas in the exposed group of animals, 45.7% (58/127), as compared with the 36.0% (80/222) in controls. These results were reported as not statistically significant.

Reeves et al (1974) exposed groups of 30 Swiss mice to dusts of crocidolite, amosite, and chrysotile for 4 hours/day, 4 days/week, for 2 years at a mean concentration of about 50 mg/m^3. Two of the animals exposed to crocidolite developed papillary carcinomas of the bronchus, as did one of the nonexposed controls.

Gross et al (1967) observed carcinomas of the lung in rats repeatedly exposed to chrysotile dust with a mean concentration of 86 mg/m^3 for 30 hours/week. Twenty of 72 rats surviving for 16 months or longer developed adenocarcinomas and 4 developed squamous-cell carcinomas, whereas no tumors occurred in 39 controls. The authors suggested that the presence of trace metals from the hammers of the mill used to prepare the fiber was a factor in causing these tumors. However, this suggestion was not confirmed by subsequent experiments (Reeves et al, 1974; Wagner et al, 1974), thus leading Gross et al (1974) to retract the trace metal hypothesis for asbestos-induced neoplasia.

Reeves et al (1971) found squamous carcinomas of the bronchus in 2 of 31 rats which survived exposure to crocidolite for 2 years at a concentration of 49 mg/m^3 for 16 hours/week. Five rats in a group of 40

exposed to chrysotile developed pulmonary adenomatosis, but no malignant tumors were observed in rats exposed to either chrysotile or amosite.

In a subsequent experiment, Reeves et al (1974) exposed groups of 69 Charles River CD rats to crocidolite, amosite, and chrysotile for 4 hours/day, 4 days/week, for 2 years, at mean concentrations of about 50 mg/m^3 (Table II-4). In addition, groups of 20 rabbits, 32 guinea pigs, and 68 gerbils were exposed for 18 months to the same three asbestos dusts as the rats mentioned above. No tumors were observed, but mean survival times were not stated.

Wagner et al (1974) exposed groups of C/D Wistar rats to the five UICC asbestos samples at concentrations of about 12 mg/m^3 of dust for 7 hours/day, 5 days/week, for several lengths of exposure: 1 day, 3 months, 12 months, and 24 months. At the end of the periods of exposure, the amount of dust in the lungs of animals exposed to the two chrysotile samples was much less than in the animals exposed to the three amphibole samples. However, all types of fiber produced asbestosis which was progressive after removal from the dust. Furthermore, whereas no tumors were found in the control group, carcinogenicity was demonstrated in the groups exposed to chrysotile (Canadian or Rhodesian) and the amphiboles (Table II-5). An increasing incidence of neoplasms was observed with increasing exposures to each form of asbestos. Even as little as 1 day of exposure - when the animals were allowed to survive and were observed - produced neoplasia (Table II-6). One-day exposures to Canadian chrysotile produced lung tumors. Mesotheliomas were observed in 11 rats, 2 of which were exposed for only 1 day, one to amosite, and one to crocidolite.

Wagner et al (1976) compared rats exposed for a 2-year period to a

pure nonfibrous cosmetic talc, with another group of rats exposed to superfine chrysotile. Similar degrees of fibrosis were found in each group while one adenocarcinoma was found in an animal exposed to the chrysotile.

(d) Fiber Analysis in Tissue

Following inhalation, asbestos fibers found in sections of lung tissue were usually <3 μm in diameter and <100 μm in length. Thicker or longer fibers were either not inhaled or were rapidly cleared from the respiratory tract. On a weight basis, only a very small proportion of inhaled fiber was retained. An account of the inhalation of fibers is given by Timbrell (1965, 1972). Electron-microscopy is essential for studies of asbestos in tissue as many of the fibers of chrysotile and amphiboles are too small in diameter to be seen with the light microscope (Langer and Pooley, 1973).

The retention of different types of asbestos in animals following exposure to the same concentrations of respirable dust was described by Wagner et al (1974). For the amphiboles, there was a similar pattern with an almost proportional increase of lung dust with the dose. Much less dust was found for the chrysotiles and no increase of dust content in the lungs was shown. Dust in the lungs of animals exposed for 6 months had been partially cleared 18 months after the inhalation period. About 74% of the amosite and crocidolite and 41% of the anthophyllite were eliminated. The elimination rate of chrysotiles could not be exactly determined because of their low content in the lung (Figure II-1) (Wagner et al, 1974).

The penetration and clearance of radioactive UICC crocidolite has been studied in rats. After 30 days, the lung content of crocidolite was

reduced to 75% of the initial value (Evans et al, 1973).

In early experiments, guinea pigs and monkeys exposed to the four commercial types of asbestos developed fibrotic lesions of the lung and pleura similar to those seen in human cases of asbestosis (Vorwald et al, 1951; Wagner, 1963; Holt et al, 1965). In more recent experiments, this finding has been confirmed in rats (Wagner et al, 1973).

The question whether asbestos fibers can move from their site of primary deposition in the body and induce cancer in other sites is still a vexing one. Volkheimer (1973) and Schreiber (1974) have reported that particles and plant fibers ingested by experimental animals and man can penetrate the wall of the gastrointestinal tract and be transported throughout the body, possibly appearing in the urine. Westlake et al (1965) fed a diet containing 6% of chrysotile to rats and reported that the animals had fibers in the wall of the colon. Cunningham and Pontefract (1973) performed a similar experiment and reported that asbestos fibers appeared in the blood and various tissues. A more recent report by Gross et al (1974) concluded, however, that there was no satisfactory evidence from their study of transmigration of fibers outside the gastrointestinal tract.

In studies in which chrysotile labelled intrinsically with radioactive trace metals by neutron irradiation was injected intrapleurally into rats, Holmes and Morgan (1967) found evidence of where a small amount of the fiber passed from the pleural cavity and lungs into such other organs as the liver. In a later, similar experiment, Morgan et al (1971) reported that a population of radionuclides, consistent with that expected on the basis of the labelled chrysotile, was found in the heart, the lungs,

the diaphragm, and the chest muscles.

Karacharova et al (1969) and Friedrichs et al (1970) found some evidence of movement of asbestos fibers from an ip site of injection into various tissues in rats. The latter group of investigators reported that movement was inversely related to the length of the fiber, becoming essentially zero for fibers 20 or more μm long.

Roe et al (1967) and Kanazawa et al (1970) found evidence of transport of asbestos fibers from subcutaneous sites of deposition to such organs as the spleen, the liver, kidneys, and the brain of mice. Cunningham and Pontefract (1973, 1974) reported that iv-injected asbestos localized mostly in the liver and the lungs. The later paper found further that chrysotile injected iv into pregnant rats crossed the placenta and appeared in the livers and lungs of the fetuses.

Mutagenicity

Sincock and Seabright (1975) found that chrysotile and crocidolite asbestos dust in a concentration of 0.01 mg/ml in culture medium induced chromosomal aberrations in Chinese hamster cells. However, these changes were not observed with glass fiber or glass powder.

REFERENCES FOR CHAPTER II

1. Miller L, Smith WE, Berlinger SW (1965): Tests for effect of asbestos on benzo(a)pyrene carcinogenesis in the respiratory tract. Ann NY Acad Sci 132:489

2. Vosame A (1972): in International Agency for Research on Cancer, Annual Report 1971. Lyon, p 46

3. Pylev LN (1972): Morphological lesions in rat lungs induced by intratracheal injection of chrysotile asbestos alone and with benzo(a)pyrene. Vopr Onkol 18:40

4. Pylev LN, Shabad LM (1973): Some results of experimental studies in asbestos carcinogenesis, in Bogovski P, Gilson JC, Timbrell V, Wagner JC (eds): Proceedings of the Conference on Biological Effects of Asbestos. Lyon, 99 pp

5. Shabad LM, Pylev LN, Krivosheeva LV, Kulagina TF, Nemenko BA (1974): Experimental studies on asbestos carcinogenicity. J Natl Cancer Inst 52:1175

6. Reeves AL, Puro HE, Smith RG, Vorwald AJ (1971): Experimental asbestos carcinogenesis. Environ Res 4:496

7. Maltoni C, Annoscia C (1973): Mesotheliomas in rats following the intraperitoneal injection of crocidolite, in Maltoni C, Davis W (eds): Characterization of Human Tumors. Proceedings of the Fifth International Symposium on the Biological Characterization of Human Tumors. Bologna. 4-6 April 1973, Voll, 115 pp

8. Pott F, Friedrichs KH (1972): Tumoren der Ratten Nach I. P. Injektion faser formiger Staube. Naturwissenschaften 59:318

9. Pott F, Huth F, Friedrichs KH (1974) Tumorigenic effect of Fibrous Dusts in Experimental Animals. Environ Health Pers 9:

10. Pott EF, Huth F, Friedrichs KH (1972): Rat tumors after intraperitoneal injection of ground chrysotile asbestos and benzo(a)pyrene zentralblatt fur bakteriologic, Parasitenkunde, Infelitionskrankheiter und Hygiene I Abt Orig, Reihe B, vol 155, no 5-6, pp 463-69

11. Wagner JC, Berry G, Timbrell V (1973): Mesotheliomata in rats after inoculation with asbestos and other materials. Br J Cancer 28:173

12. Stanton MF, Wrench C (1972): Mechanisms of mesothelioma induction with asbestos and fibrous glass. J Natl Cancer Inst 48: 797

13. Stanton MF (1973): Some aetiological considerations of fibre carcinogenesis, in Bogovski P, Gilson JC, Timbrell V, Wagner JC (eds): Proceedings of the Conference on Biological Effects of Asbestos. Lyon, 284 pp

14. Donna A (1970): Tumori sperimentali da amianto di crisotilo, crocidolite e amosite in ratto Sprague-Dawley. Med Lav 61:1

15. Smith WE, Miller L, Elsasser RE, Hubert DD (1965): Tests for carcinogenicity of asbestos. Ann NY Acad Sci 132:456

16. Groth DH, Stokinger HE, Phipps FC, Conner WL (1975): Carcinogenic Activity of Asbestos Coated with 3-4-Benzo-a-pyrene. Oral presentation at the AIHA meeting in Minneapolis, Minnesota, 5 June

17. Wagner JC, Berry G (1969): Mesotheliomas in rats following inoculation with asbestos. Br J Cancer 23:567

18. Harrington JS (1962): Occurrence of oils containing 3:4-benzopyrene and related substance in asbestos. Nature (London) 193:43

19. Harrington JS, Roe FJC (1965): Studies of carcinogenesis of asbestos fibres and their natural oils. Ann NY Acad Sci 132:439

20. Roe RJC, Walters MA, Harrington JS (1966): Tumor initiation by natural and contaminating asbestos oils. Int J Cancer 1:491

21. Commins BT, Gibbs GW (1969): Contaminating organic material in asbestos. Br J Cancer 23:358

22. Morgan A, Holmes A (1970): Neutron activation techniques in investigations of the composition and biological effects of asbestos, in Shapiro HA (ed): Pneumoconiosis. Proceedings of the International Conference, Johannesburg. Cape Town, Oxford University Press, p 52

23. Morgan A, Holmes A, Gold C (1971): Studies of the solubility of constituents of chrysotile asbestos in vivo using radioactive tracer techniques. Environ Res 4:558

24. Kanazawa K, Birbeck MSC, Carter RL, Roe FJC (1970): Migration of asbestos fibres from subcutaneous injection sites in mice. Br J Cancer 24:96

25. Timbrell V, Rendall REG (1972): Preparation of the UICC standard reference samples of asbestos. Powder Technol 5:279

26. Occella E, Maddalon G (1963): X-ray diffraction characteristics of some types of asbestos in relation to different techniques of comminution. Med J Lav 54:628

27. Wagner JC, Berry G, Cooke TJ, Hill RJ, Pooley FD, Skidmore JW (1976): Animal experiments with talc. Fourth International Symposium on Inhaled Particles and Vapors, Edinburgh, September 1975 (in press)

28. Wagner JC, Berry G, Skidmore JW (1975a): Studies of the carcinogenic effect of fibre glass of different diameters following intrapleural inoculation in experimental animals. NIOSH Symposium on Occupational Exposure to Fibrous Glass, University of Maryland, June 1974, HEW publication No. (NIOSH) 76-151. Dept of Health, Education, and Welfare, Public Health Service, Center for Disease Control, NIOSH, April 1976, pp 193-197

29. Gross P, Harley A, Swinburne LM, Davis JMG, Greene WB (1974): Ingested mineral fibers. Do they penetrate tissue or cause cancer? Arch Environ Health 29:341

30. Lynch KM, McIver FA, Cain JR (1957): Pulmonary tumours in mice exposed to asbestos dust. Arch Ind Health 15:207

31. Reeves AL, Puro HE, Smith RG (1974): Inhalation carcinogenesis from various forms of asbestos. Environ Res 8:178

32. Gross P, deTreville RTP, Tolker B, Kaschak M, Babyak MA (1967): Experimental asbestosis. The development of lung cancer in rats with pulmonary deposits of chrysotile asbestos dust. Arch Environ Health 15:345

33. Wagner JC, Berry G, Skidmore JW, Timbrell V (1974): The effect of the inhalation of asbestos in rats. Br J Cancer 29:252

34. Timbrell V (1965): The inhalation of fibrous dusts. Ann NY Acad Sci 132:255

35. Timbrell V (1972): Inhalation and biological effects of asbestos, in Mercer TT, Morrow PE, Stober W (eds): Assessment of Airborne Particles. Proceedings of the Third Rochester International Conference on Environmental Toxicity, Rochester, Springfield, Ill., Thomas, p 429

36. Langer AM, Pooley FD (1973): Identification of single asbestos fibres in human tissues, in Bogovski P, Gilson JC, Wagner JC (eds): Proceedings of the Conference on Biological Effects of Asbestos, Lyon, p 119

37. Evans JC, Evans RJ, Holmes A, Hounam RF, Jones DM, Morgan A, Walsh M (1973): Studies on the deposition of inhaled fibrous material in the respiratory tract of the rat and its subsequent clearance using radioactive tracer techniques - I. UICC crocidolite asbestos. Environ Res 6:180-201

38. Vorwald AJ, Durkan TN, Pratt PC (1951): Experimental studies of asbestosis. Arch Ind Hyg 3:1

39. Wagner JC (1963): Asbestosis in experimental animals. Br J Ind Med 20:1

40. Holt PF, Mills J, Young DK (1965): Experimental asbestosis with four types of fibers: Importance of small particles. Ann NY Acad Sci 132:87

41. Sincock A, Seabright M (1975): Induction of chromosome changes in Chinese hamster cells by exposure to asbestos fibres. Nature 257:56

42. Volkheimer G (1973): Persorption. Acta Hepato-Gastroenterol 20:361

43. Schreiber G (1974): Ingested dyed cellulose in the blood and urine of man. Arch Environ Health 29:39-42

44. Westlake GE, Spjict HJ, Smith MN (1965): Penetration of colonic mucosa by asbestos particles. Lab Invest 14:2029-33

45. Cunningham HM, Pontefract RD (1973): Asbestos in beverages, drinking water and tissues: their passage through the intestinal wall and movement through the body. J Assoc Agric Chem 56:976-81

46. Holmes A, Morgan A (1967): Leaching of constituents of chrysotile asbestos in vivo. Nature 215:441-42

47. Karacharova VN, Ol'Shavang RA, Kogan FM (1969): Changes in certain organs after experimental intraperitoneal injection of asbestos-containing dust. Byull Eksp Biol Med 67:117-120

48. Friedrichs KH, Hilscher W, Setki S (1971): Fiber and tissue studies on rats after intraperitoneal injection of asbestos. Arch Arbeitsmed 28:341-54

49. Roe FJC, Cartes RL, Walters MA, Harrington JS (1967): The pathological effects of subcutaneous injections of asbestos fibers in mice: Migration of fibers to submesothelial tissues and induction of mesotheliomata. Int J Cancer 2:628-38

50. Cunningham HM, Pontefract RD (1974): Placental transfer of asbestos. Nature 249:177-78

SUMMARY TABLE OF ASBESTOS-INDUCED CARCINOGENICITY IN ANIMALS

Author	Date	Finding	Type of Animal	Dosage	Type of Fiber
INTRATRACHEAL INSTILLATION					
Miller	1965	Tumors of respiratory tract	Hamster	Unknown	Chrysotile with benzo (a) pyrene
Vosamae	1972	"	Rats	"	"
Pylev	1972	"	"	"	"
Pylev & Shabad	1973	"	"	"	"
Shabad et al	1974	Lung papillomas, epidermoid carcinomas reticulosarcomas, pleural mesotheliomas 6/21 and 6/11 rats within 9-28 mon	"	2 mg Russian chrysotile 5 mg benzo (a) pyrene	Russian chrysotile
INTRAPERITONEAL ADMINISTRATION					
Reeves et al	1971	3/13 peritoneal mesotheliomas with chrysotile 3/13 peritoneal mesotheliomas with crociodolite 0/11 peritoneal mesotheliomas with amosite After 7-17 mon	"	0.3, 0.5 or 1.0 ml of solution of 20 mg/ml.	Amosite Crocidolite Chrysotile
Maltoni	1973	31/50 mesothelioma in males 34/50 mesothelioma in females	Sprague-Dawley rats (18 wk old)	25 mg crocidolite	Crocidolite
Potts and Friedrichs	1972	40% tumor occurrence	Wistar rats	2, 6.25, 25, 75, 100 mg	Chrysotile A
Pott	1974	"	"	2, 10, 50 mg	"

SUMMARY TABLE OF ASBESTOS-INDUCED CARCINOGENICITY IN ANIMALS (CONTINUED)

Author	Date	Finding	Type of Animal	Dosage	Type of Fiber
INTRAPLEURAL ADMINISTRATION					
Wagner	1973	61% tumors with crocidolite 36% tumors with amosite 34% tumors with anthophyllite 30% tumors with Canadian chrysotile 19% tumors with Rhodesian chrysotile	Rats	20 mg	Crocidolite Amosite Anthophyllite Canadian chrysotile Rhodesian chrysotile
Stanton and Wrench	1972	Mesotheliomas in 60% rats	"	40 mg	Crocidolite Amosite and Rhodesian chrysotile
Pylev and Shabad	1973	Mesotheliomas	"	60 mg	Russian chrysotile
Groth et al	1975	No mesotheliomas-but animals killed 90-150 d after injection-insufficient latent period	Albino rats	Unknown	
Wagner	1976	18/48 mesotheliomas- 0/48 mesotheliomas-talc	Rats		Chrysotile Talc
Reeves et al	1971	1/15 mesothelioma with crocidollte 2/12 mesothelioma with chrysotile	"	.5 ml	Amosite Crocidolite Chrysotile
Reeves et al	1971	2/13 mesothelioma with chrysotile	Rabbit	.8 ml	Chrysotile
Shabad et al	1974	31/67 mesotheliomas within 2 yr	Rats	20 mg	Russian chrysotile

SUMMARY TABLE OF ASBESTOS-INDUCED CARCINOGENICITY IN ANIMALS (CONTINUED)

Author	Date	Finding	Type of Animal	Dosage	Type of Fiber
INGESTION					
Gross et al	1974	No significant difference in tumor incidence observed; survival rates not reported sample sizes were small	Rats	5% fiber by weight in food	Chrysotile and Crocidolite
Wagner et al	1976	2 gastric leiomyosarcomas, 1 in animal fed talc and 1 fed chrysotile	32 Wistar SPF rats	100 mg/d/ 5 d/wk 100 d over a 6-mon period	Chrysotile or Talc
INHALATION					
Lynch et al	1957	45.7 (58/127) pulmonary adenomas in exposed group 36.0% (80/222) pulmonary adenomas in controls	AC/F hybrid mice	Dust concentrations ranged from 150,000,000 to 300,000,000 particles per cc.	Chrysotile
Reeves et al	1974	2/30 bronchiogenic carcinoma with chrysotile	Swiss mice	50 mg/m^3 4 hr/d, 4 d/wk for 2 yr	Crocidolite Amosite Chrysotile
Gross et al	1967	20/72 rats surviving 16 mon or longer developed adeno-carcinomas 4/72 rats developed squamous-cell carcinomas 0/39 tumors in controls	Rats	86 mg/m^3 for 30 hr/wk	Chrysotile dust
Reeves et al	1971	2/31 rats developed carcinoma of the bronchus with crocidolite exposure 3/40 rats developed adenomatosis with chrysotile exposure	"	49 mg/m^3 for 16 hr/wk for 2 yr	Crocidolite Chrysotile Amosite

SUMMARY TABLE OF ASBESTOS-INDUCED CARCINOGENICITY IN ANIMALS (CONTINUED)

Author	Date	Finding	Type of Animal	Dosage	Type of Fiber
INHALATION					
Wagner et al	1974	Asbestosis produced with all types of fibers	C/D Wistar rats	12 mg dust hr/d -- d/wk for several lengths of exposure (1 d, 3 mon, 12 mon, 24 mon)	Chrysotile Amosite
		Lung Cancer / Mesothelioma / Fiber			
		11/146 / 1/146 / amosite			
		16/145 / 2/145 / anthophyllite			
		16/141 / 4/141 / crocidolite			
		17/137 / 4/137 / chrysotile (Canadian)			
		30/144 / 0/144 / chrysotile (Rhodesian)			
Sincock and Seabright	1975	Chromosal abberation in Chinese hamster cells	Hamster	0.01 mg/ml	Chrysotile Crocidolite

TABLE II-1

TUMORS IN ABDOMEN AND/OR THORAX AFTER INTRAPERITONEAL INJECTION OF DIFFERENT FIBROUS AND GRANULAR DUSTS

Dust	Form*	Dose i.p. (mg)	Effective Number of Dissected Rats	First Tumor After ... Days	Average Survival Time of Rats with Tumors (days after inj.)	Rats with Tumor (%)
Chrysotile A UICC	f	2	37	431	651	16.2
"	f	6.25	35	343	501	77.1
"	f	25	31	276	419	80.6
"	f	4 x 25	33	323	361	54.5
"	f	3 x 25	33	449	449	3.0
" milled	f	4 x 25	37	400	509	32.4
Palygorscite	f	3 x 25	34	257	348	76.5
Glass fibers S + S 106	f	2	34	692	692	2.9
"	f	10	36	350	530	11.1
"	f	4 x 25	32	197	325	71.9
Gypsum	f	4 x 25	35	579	583	5.7
Nemalite	f	4 x 25	34	249	315	73.5
Actinolite	g	4 x 25	39	-	-	-
Biotite	g	4 x 25	37	-	-	-
Haematite (precipit.)	g	4 x 25	34	-	-	-
Haematite (mineral)	g	4 x 25	38	-	-	-
Pectolite	g	4 x 25	40	569	569	2.5
Sanidine	g	4 x 25	39	579	579	2.6
Talc	g	4 x 25	36	587	587	2.8
NaCl-Control	-	4 x 2m	72	-	-	-

*f = fibrous
g = granular
From Potts and Friedrichs (1972)

TABLE II-2

TUMORS IN ABDOMEN AND/OR THORAX AFTER INTRAPERITONEAL INJECTION OF GLASS FIBERS, CROCIDOLITE AND CORUNDUM

Dust	Form*	Dose i.p. (mg)	Effective Number of Dissected Rats	First Tumor After ... Days	Average Survival Time of Rats with Tumors (days after inj.)	Rats with Tumor (%)
Glass fibers						
MN 104	f	2	73	421	703	27.4
"	f	10	77	210	632	53.2
"	f	2 x 25	77	194	367	71.4
Glass fibers						
MN 112	f	20	37	390	615	37.8
Crocidolite	f	2	39	452	761	38.5
Corundum	g	2 x 25	37	545	799	8.1

*f = fibrous
g = granular
From Pott et al (1974)

TABLE II-3

PERCENTAGE OF RATS DEVELOPING MESOTHELIOMAS AFTER INTRAPLEURAL INOCULATION OF VARIOUS MATERIALS

Material	Percentage of rats with mesotheliomas
SFA Chrysotile	66
UICC crocidolite	61
UICC amosite	36
UICC anthopyllite	34
UICC chrysotile (Canadian)	30
UICC chrysotile (Rhodesian)	19
Fine Glass Fibre (code 100)	12
Ceramic fibre	10
Glass powder	3
Coarse glass fiber (code 110)	0

From Wagner et al (1976)

TABLE II-4

INHALATION CARCINOGENESIS FROM VARIOUS FORMS OF ASBESTOS

Form of Asbestos	Number of Tumors
Controls	no tumors
Amosite	2 pleural mesotheliomas
Crocidolite	3 squamous-cell carcinoma, 1 papillary carcinoma and 1 adenocarcinoma, all of lungs.
Crysotile	1 papillary carcinoma, 1 squamous-cell carcinoma of lungs, and 1 pleural mesothelioma.

From Reeves et al (1974)

TABLE II-5

NUMBER OF ANIMALS WITH LUNG TUMORS OR MESOTHELIOMA ACCORDING TO TYPE OF ASBESTOS

Dust	No. of Animals	Tumor Type		
		Adenocarcinoma	Sq. Carcinoma	Mesotheliomas
Controls	126	0	0	0
Amosite	146	5	6	1
Anthopyllite	145	8	8	2
Crocidolite	141	7	9	4
Chrysotile (Canadian)	137	11	6	4
Chrysotile (Rhodesian)	144	19	11	0

From Wagner et al (1974)

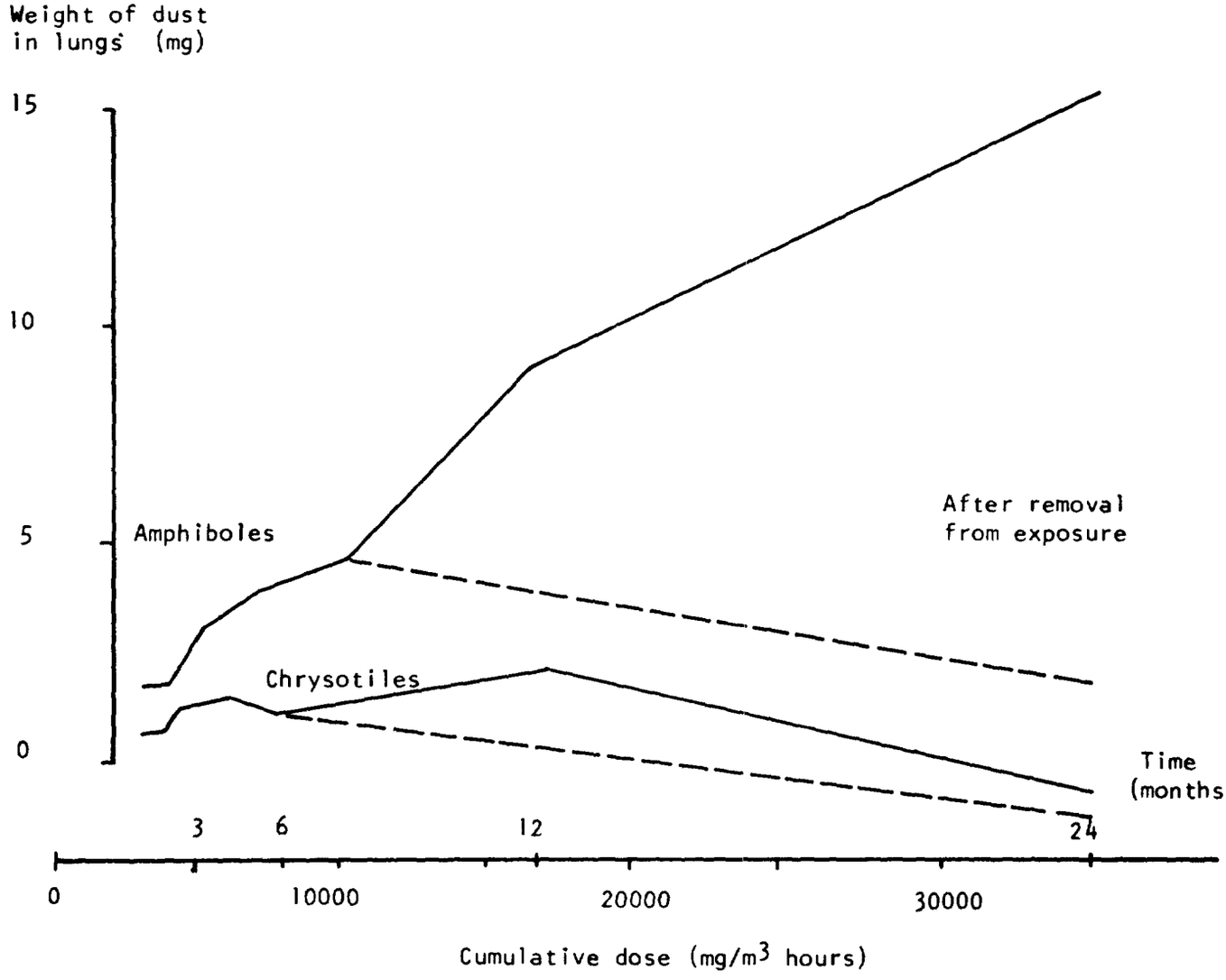
TABLE II-6

NUMBER OF ANIMALS WITH LUNG TUMORS OR MESOTHELIOMA ACCORDING TO LENGTH OF EXPOSURE

Length of Exposure	No. of Animals	No. with Lung CA	No. with Pleural Mesotheliomas	% of Animals with Tumors
Controls	126	0	0	0.0
1 d	219	3	2	2.3
3 mon	180	8	1	5.0
6 mon	90	7	0	7.8
12 mon	129	35	6	31.8
24 mon	95	37	2	41.0

From Wagner et al (1974)

Effects of Inhalation of Asbestos in Rats



Mean weight of dust in lungs of rats in relation to dose and time.
from Wagner et al (1974)

FIGURE II-1

III. EFFECTS ON HUMANS

Nonmalignant Respiratory Diseases

(a) Historical Studies

The use of asbestos dates back thousands of years; however, the modern industry dates from about 1880, when it was used to make heat and acid resistant fabrics, (Hendry, 1965; Hueper, 1966). With the increasing use of asbestos materials, reports of asbestos-related disease emerged.

The first record of a case of asbestosis was reported in England by Montague Murray in 1906. Hoffman (1918) reported that it was the practice of American and Canadian insurance companies not to insure asbestos workers due to unhealthful conditions in that industry. Pancoast et al (1917) commented on x-ray changes resembling pneumoconiosis in 15 individuals exposed to asbestos. The first complete description of asbestosis and of the "curious bodies" seen in lung tissue appeared when Cooke (1927) reported on a case of asbestosis, and McDonald (1927) reported on the same and another case. Each author gave reasons for believing that these "curious bodies" originated from asbestos fibers that had reached the lungs. Mills (1930) reported the first case of asbestosis in the United States, and in the same year, Lynch and Smith (1930) reported on "asbestosis bodies"* found in the sputum of asbestos workers. Early studies led many investigators to conclude that people exposed to asbestos

*"Ferruginous bodies" is a more descriptive term, as other inhaled fibers, eg, fibrous glass, may also become iron coated.

dust developed the disease "asbestosis" if the dust concentration was high or their exposure was long (Merewether and Price, 1930; Merewether, 1934; Fulton et al 1935; Dreessen et al, 1938).

(b) Epidemiologic Studies

Harries (1968) reported that although first impressions would lead one to believe that only workers continuously exposed to asbestos are at risk of developing asbestosis, further consideration of the industry and processes should have suggested that many other workers were also at risk. For example, some trades worked in confined spaces where asbestos was used. Work in shipboard trades was accepted by the Pneumoconiosis Panel of the United Kingdom as associated with asbestosis.

Murphy et al (1971a) found that asbestosis was 11 times more common among pipe insulators involved in new ship construction than among a control group. Asbestosis first appeared 13 years after exposure or at about 60 mppcf-years. The prevalence was 38% after 20 years. They also reported a case of extensive pleural calcification in a worker whose only known asbestos exposure was during sanding asphalt and vinyl tile floors (Murphy et al, 1971b).

Lorimer et al (1976), in a study of brake repair and maintenance workers exposed to asbestos, found that 25% of the workers showed evidence of x-ray abnormalities consistent with asbestosis. One quarter also had restrictive pulmonary function test findings.

Meurman et al (1973) found a three-fold risk of dyspnea and a two-fold risk of cough for asbestos workers as compared with controls, after adjusting for smoking.

Weill et al (1975) reported a decreased lung function in relation to

increasing cumulative dust exposure in a group of asbestos cement manufacturing workers. Ayer and Burg (1976) reported a decrease in pulmonary function in asbestos textile workers with less than ten years of exposure.

In a study of 232 former insulation plant employees, Selikoff (1976a) reported positive x-ray findings among individuals having exposures to asbestos known to be as short as 1 day. More recently, Anderson et al (1976) reported x-ray findings consistent with asbestosis in household and family members having no known exposure to asbestos other than residing with a known asbestos worker. These two studies demonstrate the presence of asbestos disease in the absence of continuing new known exposures.

Wagoner et al (1973) demonstrated a significantly increased risk of death from nonmalignant respiratory disease and for diseases of the heart, which in part were secondary to pulmonary disease, among a cohort of workers in a major manufacturing complex using predominately chrysotile. Among those workers observed 20 or more years after onset of employment, a four-fold increased risk of death due to nonmalignant respiratory disease was observed. Further evaluation of these deaths revealed that the majority occurred within 1 year after termination of employment and at an average age of 53.8 years.

Newhouse (1969) reported an increased risk of death from nonmalignant respiratory disease in male asbestos textile and insulation workers with low to moderate exposure.

Enterline and Henderson (1973) reported that for all ages, only 18 deaths from asbestosis occurred in several asbestos plants studied from 1941 to 1969. It is significant to note, however, that the state of New

Jersey alone, in the years 1969-1970, had awarded workman's compensation for asbestosis to 455 workers from one of the plants in the study. (Heymann, 1971; Serraino, 1970)

Selikoff (1976a) reported a significant excess of deaths due to asbestosis among a group of workers in the US and Canada. Out of 17,800 asbestos insulation workers, there were 119 observed deaths attributed to asbestosis. Although it was not reported, the expected death rates from asbestosis in the general population would be virtually zero.

(c) Description of Asbestosis

Asbestosis is a chronic lung disease due to the inhalation of asbestos fibers and is characterized by diffuse interstitial fibrosis, frequently associated with pleural fibrosis (thickening) or pleural calcification.

The characteristic x-ray changes of asbestosis are small irregular opacities in the lower and middle lung fields, often accompanied by pleural thickening and pleural calcifications.

The pulmonary fibrotic changes develop slowly over the years--often progressively even without further exposure--and their radiographic detection is a direct correlate of their extent and profusion. In some cases, minor fibrosis with considerable respiratory impairment and disability can be present without equivalent x-ray changes. Conversely, extensive radiographic findings may be present with little functional impairment.

Commonly found in asbestosis are pulmonary rales, dyspnea, finger clubbing and cyanosis, but any or all can be absent in any one case.

Pulmonary hypertension is frequently associated with advanced

asbestosis and the resultant cor pulmonale (right-sided heart failure) may be the cause of death.

Carcinogenicity

(a) Occupational Exposure

(1) Historical Studies

In 1935, 55 years after the start of large-scale usage of asbestos in industry, suspicion of an association between asbestosis and lung cancer was reported by Lynch and Smith (1935) in the USA and by Gloyne (1935) in the UK. About 10 years later, case reports of pleural and peritoneal tumors associated with asbestos appeared (Wedler, 1943, a,b; Wyers, 1946). Epidemiologic evidence from Doll (1955) showed a ten-fold excess risk of lung cancers in those UK asbestos textile workers who had been employed before 1930, before regulations produced improved dust conditions in factories. Similar findings were reported in the USA in 1961. Mesotheliomas were also detected but this fact was not published until later (Mancuso and Coulter, 1963; Selikoff et al, 1964). Possible variations in risk with different types of fiber were rarely considered in the early reports. Since 1964, following the recommendations of the UICC Working Group on Asbestos Cancers (UICC 1965) for new studies, there has been an expansion of epidemiologic studies in many parts of the world.

(2) Epidemiologic Studies

(A) Lung Cancer, Pleural and Peritoneal Mesotheliomas

(i) Mixed Types of Fiber

In most industrial processes different types of fiber are mixed, so that pure exposures to a single asbestos type are rare. Mortality studies of defined populations of asbestos-manufacturing,

insulating, and shipyard workers have provided the most concrete evidence concerning the association between bronchial cancer, pleural, and peritoneal mesotheliomas and exposure to asbestos. Reports have come from several countries: (UK) Newhouse, 1969; (FRG) Bohlig et al, 1970; (USA) Selikoff et al, 1970; (UK) Elmes and Simpson 1971; (The Netherlands) Stumphius, 1971; (Italy) Rubino et al, 1972.

A seven-fold excess of lung cancer was found in a group of insulation workers whose exposures had been to chrysotile and amosite but not crocidolite (Selikoff et al, 1971). Enterline and Henderson (1973) reported a 4.4 times increased risk of respiratory cancer mortality among retired men who had worked as production or maintenance employees in the asbestos industry and who had been exposed to mixed fibers. Among men with mixed exposure to crocidolite and chrysotile in the asbestos cement industry, the rate was 6.1 times the expected rate. In a British naval dockyard population, Harries (1976) showed that there had been a steep rise in mesotheliomas since 1964. However, the full biologic effects of asbestos in shipyard workers would not have been expected to be detected until the 1970's and thereafter (Selikoff, 1976a).

Edge (1976) reported that shipyard workers with mixed asbestos exposure and pleural plaques (without evidence of pulmonary fibrosis) had a 2.5 times increased risk of developing carcinoma of the bronchus, when compared with matched controls without plaques. In a study of sheet metal workers (Cooper et al, 1975) with measurable and mixed asbestos exposure, an excess of deaths from malignant neoplasms (24.7% of deaths for two cohorts selected for 5 or more years worked in the trade, 19.1% of deaths for a group with death claims where 14.5% was expected) was

largely attributed to an excess of malignant tumors of the respiratory tract. Of the 307 deaths in the first cohort, 32 lung cancer deaths were significantly in excess (1.7 times the expected). One pleural mesothelioma was observed.

Additional confirmatory evidence of the association between mesotheliomas and past exposure to asbestos comes from many institutes and departments of pathology and cancer registers, eg, (France) DeLarjarte et al, 1973; (Italy) Gobbato and Ferri, 1973; (South Africa) Webster, 1973; (UK) Greenberg and Lloyd Davies 1974; (FRG) Hain et al, 1974; (Finland) Nurminen and Markku), (German Democratic Republic) Sturm, 1975; (The Netherlands) Zielhuis et al, 1975). These studies have shown an association between asbestos and mesothelioma even with exposures as brief as 1 day; however, approximately 15% of the mesotheliomas are not known to be related to exposure to asbestos. Three studies (McDonald et al, 1973; Greenberg and Lloyd Davies, 1974; Newhouse et al, 1972) showed a poor correlation between certified cause of death and histologic diagnosis of mesothelioma. There is still a need to reduce the inter-observer variation in the diagnosis of these rare and pleomorphic tumors (McCaughey and Oldham, 1973).

The ratio of pleural to peritoneal tumors appear to be associated with heavier exposures (Newhouse et al, 1973). Among a number of occupationally exposed groups studied, approximately 5 - 7% of deaths have been from mesotheliomas (Gilson, 1973; Hammond and Selikoff, 1973; Selikoff, 1976b). More recently however, an estimate has projected that 11% of asbestos workers' deaths in England will be from mesotheliomas

(Newhouse and Berry, 1975).

(ii) Individual Types of Fibers

Crocidolite - In 1956, Wagner started investigating the occurrence of pleural and peritoneal mesotheliomas in the crocidolite mining areas of the Northwest Cape Province in South Africa. It was shown that these tumors occurred in the nonmining population living in the vicinity as well as among men working in the mines and mills and in the transportation and handling of the fiber (Wagner, 1960). Asbestosis was not invariably present. The latent period between first exposure and clinical recognition of the tumor was long - a mean of 40 years. Subsequent surveillance of the mining population in all the asbestos-producing areas in South Africa has added support for a major difference in the incidence of mesotheliomas within the crocidolite mining areas of that country. (Harrington et al, 1971; Webster, 1973). The mining of crocidolite in northwest Australia has been associated with mesotheliomas (McNulty 1962). Jones et al (1976) have reported a high incidence of mesotheliomas among women who worked with crocidolite in a factory producing gas mask canisters during World War II.

Chrysotile - McDonald et al (1973, 1974) reported that the overall death rate among 11,500 workers born between 1891 and 1920 and employed in the chrysotile mines and mills of Quebec was lower than for Quebec Province as a whole. An increased lung cancer risk was found and considered to be dose-related, and those who had been most heavily exposed to the dust showed about a five-fold risk compared with the least exposed. Of the 3,270 deaths, 134 were from respiratory cancer, with 129 being lung cancer and 5 mesotheliomas. Recently, the authors (McDonald

and McDonald, 1976) have observed 3,938 total deaths among males through 1973, of which 224 were from lung cancer and 7 from mesothelioma. The authors suggested that the respiratory cancer mortality in the Quebec chrysotile industry as a whole was greater than that expected on the basis of regional mortality data.

Kogan et al (1972) investigated the cancer mortality among workers in asbestos mining and milling industries between 1948 and 1967. The total cancer mortality rate among workers was 1.6 times higher than that found in the general male population; for female workers the rates were 0.8 for those in mines and 1.3 for those in mills. The lung cancer risk for male miners and millers was twice that of the general male population. For females in mines and mills, the risks were 2.1 and 1.4 times that of the general female population, respectively. For those workers over 50 years of age, the risk of lung cancer was greater: for men in mining, 4.9; those in milling, 5.9; for women in mining, 9.5; and for those women in milling, 39.8 times that found in the general population. No mesotheliomas were found, but Kogan et al (1972) indicate that this might be explained by the insufficient experience of pathologists with this rare type of cancer in that geographical area. Also, the number of people in the study populations were not reported.

Wagoner et al (1973) reported on the cancer risk among a cohort of workers in a major manufacturing complex utilizing predominately chrysotile asbestos in textile, friction, and packaging products. An excess of respiratory cancer occurred among asbestos workers in each duration-of-employment category down to and including 1-9 years. They observed statistically significant standard mortality ratios of 122

for all malignant neoplasms and 244 for malignant neoplasms of the respiratory system. The asbestos workers in this study were located in an area of predominately Amish Dutch population with known low frequencies of smoking. The authors, nevertheless, used the general white male US population as a control group, which would tend to underestimate the degree of risk.

Enterline and Henderson (1973) found that for retired men who had worked as production or maintenance employees in the asbestos industry and who had reached 65 years of age, those who had been exposed only to chrysotile had a respiratory cancer risk two - four times than that expected. Among men within the asbestos cement industry exposed only to chrysotile, a one- to four-fold excess of respiratory cancer was found. Of 802 deaths, only one mesothelioma had been recorded in the several plants investigated. In contrast, a subsequent investigation by Borow et al (1973) found 70 cases of mesothelioma from only one of these plants. The discrepancy was due to methodologic variations, for example, Enterline and Henderson (1973) had limited their investigation to men age 65 or over, while many of the mesothelioma cases reported by Borow et al (1973) had died before that age.

Amosite - In a study of a group of miners exposed to amphibole fibers in the cummingtonite-grunerite ore series, Gillman et al (1976) demonstrated mortality from malignant respiratory disease to be three times than that found in the general population.

Exposures to amosite alone in a factory making insulation material were reported by Selikoff (1976 a & b). Ten mesotheliomas were found in addition to an increased risk of lung cancer in

workers who were observed 20 years or longer. The excess lung cancer risk in the amosite workers was shown to increase with duration of employment. There was a three-fold increase in lung cancer among those with less than 3 months employment and among those with less than 1 month employment there was a 2.25-fold increase.

In a retrospective study of 914 men who had worked periodically during World War II in a plant manufacturing insulating materials from amosite for the US Navy, Seidman et al (1976) concluded that the group of 65 men who had worked for less than 1 month had experienced excess mortality, on the age-specific basis, from lung cancer during the 30 years since the beginning of their exposure, but not from all cancers or all causes of death. Men who had worked for a full month or longer had excess mortalities from all three causations examined, the risk of death from lung cancer increasing with duration of exposure.

Anthophyllite - In Finland, anthophyllite mining has been associated with an excess bronchial cancer risk of 1 - 4 times the expectation overall, and about double this figure for those with more than 10 years' exposure (Meurman et al, 1974).

There was also a higher prevalence of dyspnea and cough in the miners. However, no mesotheliomas were found despite the presence in Finland of an unusually high incidence of pleural thickening and calcification as detected by radiographic and pathologic surveys (Kiviluoto, 1960; Meurman, 1966).

(B) Other Types of Cancer

Epidemiologic studies of the already defined populations have consistently shown an excess risk of other cancers,

especially of the gastrointestinal tract (Mancuso and El Attar, 1967; Elmes and Simpson, 1971; Kogan et al, 1972; Newhouse, 1973; Wagoner et al, 1973; McDonald et al, 1974; Selikoff et al, 1974); however, it has been less than that of lung cancers.

Schneiderman (1974), in a literature review with an emphasis on dose-response, concluded that "good dose-response data, with quantitative estimates of dose are uncommon; however, in all the literature reviewed, only one paper did not support the conclusion that increased exposure to inhaled asbestos particles leads to increased digestive system cancer."

Stell and McGill (1973) found that out of 100 men with squamous carcinoma of the larynx, 31 had known exposure to asbestos compared with only three in matched controls. Similar associations have been reported by Morgan and Shettigara (1976). Newhouse and Berry (1973) found two cases of cancer of the larynx (ICD 161) in their cohort of over 4,000 workers compared with an expected 0.4.

(b) Nonoccupational Exposure

Household contact with asbestos is associated with an increased mesothelioma risk. Anderson et al (1976) have recently reviewed 34 such cases of mesothelioma from nine countries and reported four new cases among the traced family members of 1,664 asbestos workers. Cases of mesotheliomas have also occurred in nonoccupationally exposed individuals living in the neighborhood of industrial sources of asbestos (Wagner et al, 1960; Newhouse and Thompson, 1966; Bohlig and Hain, 1973). Studies of the geographical distribution of cases of mesothelioma in the UK over a 10-year period indicate that the new cases are nearly all from areas in which there

has been a recognized industrial source of asbestos (Gilson, 1970; Greenberg and Lloyd Davies, 1974).

Lesions among nonoccupationally exposed persons in Finland have been reported where anthophyllite asbestos is mined. In this study, 118 cases of the total 126 cases of roentgenologically-diagnosed pleural calcification studied, excluding those individuals with hemothorax, emphysema, and tuberculosis, lived or have lived in areas immediately adjacent to asbestos mines (Kiviluoto 1960). The results of this study suggest a health hazard from community exposure to ambient asbestos.

SYNERGISM

There is marked enhancement of the risk of lung carcinoma in those workers exposed to asbestos who also smoke cigarettes (Selikoff et al, 1968; Doll, 1971; Berry et al, 1972; Hammond and Selikoff, 1973); Hammond and Selikoff (1973) interpret the excess lung carcinoma risk from asbestos in nonsmokers to be small. No link between cigarette smoking and mesotheliomas has been observed in a prospective study by Hammond and Selikoff (1973). A preliminary study (Lemen, 1976) on female workers employed between January 1940 and December 1967, in a predominately chrysotile asbestos textile plant, revealed 7 lung cancer deaths among 580 women when only 0.63 deaths were expected ($p<0.01$). One lung cancer death was observed in a smoker, two in women of undetermined smoking history, and four in "never" smokers as determined from hospital admission charts.

It is important to note that the historic documentation of cigarette consumption patterns is lacking for most retrospective cohort studies of asbestos workers. It is further important to note that a sizable portion of the general population, the group usually selected for comparison in

these studies, are cigarette smokers. Therefore, the risk of lung cancer demonstrated for these industrial groups exposed to asbestos is of such magnitude as to preclude the identification of an independent etiologic role for cigarette smoking.

FIBER ANALYSIS IN TISSUE

The physical characteristics of asbestos fibers which penetrate to the lung parenchyma have been studied by Timbrell (1965 and 1972) who demonstrated fiber respirability to be largely a function of fiber diameter.

Two kinds of data are relevant. Timbrell et al (1971) and Timbrell (1972) have shown that the crocidolite mined in Northern Cape Province, South Africa, and in Western Australia is associated with a high incidence of pleural mesothelioma among the local populations and has finer and shorter fibers than the crocidolite or amosite mined in the Transvaal Province, which is associated with a relatively lower incidence of pleural mesothelioma among the exposed population. As crocidolite and amosite are similar in chemical composition, there is reason to assume that the risk difference may be attributable to the differing physical characteristics of fibers.

Preliminary studies (Fondimare et al, 1974) concerning diameter and length of 5,000 asbestos fibers from the lungs of 10 deceased persons who had been occupationally exposed, showed that these fibers were all less than 0.5 μm micrometer in diameter. When separated according to type of asbestos, 90% of chrysotile fibers and 70% of amphibole fibers were less

than 5 μm in length.

Asbestos bodies have been found in large numbers by light microscopy in occupationally exposed individuals (Ashcroft and Heppleston, 1973). Numerous asbestos fibers, either of chrysotile or amphibole or both types, have been found by electron microscopy in lungs of industrially exposed men (Pooley, 1972, 1973; Fondimare et al, 1974). A quantitative topographic study of asbestos fibers in the lung has been carried out in 12 industrially exposed men which showed that heavily exposed cases with lung fibrosis and carcinomas had fewer fibers in the fibrotic lower lobes than in the less fibrotic type. In less exposed cases with lung cancer but without lung fibrosis, a higher concentration of asbestos fibers, mostly of the chrysotile type, was clearly demonstrated in peripheral areas of the lung.

Optical and electron microscopic study of pleural plaques revealed the presence of some coated fibers and large numbers of uncoated fibers, mostly short, ultimate fibrils of chrysotile (Fondimare et al, 1974).

Pooley (1973) found that 93% of 120 mesothelioma cases studied had asbestos fibers in their lungs visible by electron microscopy versus less than 50% of 135 nonmesothelioma cases. Higher concentrations of fibers were observed in mesothelioma than in nonmesothelioma cases. In mesothelioma cases, the fiber types were either amphibole or chrysotile, or both, but amphibole was predominant; in nonmesothelioma cases, chrysotile fibers were predominant. In the three cases included in the study by Fondimare et al (1974), the percentage of chrysotile fibers was from 44 to 97% in the peripheral areas of the lung. The ratio of amphibole to chrysotile has been found to decrease from the central toward the

peripheral areas of the lung (Fondimare et al, 1974; LeBouffant et al, 1976).

Coated fibers ("asbestos" or "ferruginous bodies") have been found in the lungs of most adults who have lived in urban areas (Gross et al, 1969; Bignon and Goni, 1969; Selikoff et al, 1972; Thompson et al, 1966; Davis and Gross, 1973; Oldham, 1973). The number of coated fibers in the lung has been compared in cases with and without lung carcinoma. Meurman (1966), who took cigarette consumption into account, could find no significant difference.

Doniach et al (1975) found an increased incidence of asbestos bodies in men with stomach cancer and in women with breast cancer, but not in lung cancer cases. Warnock and Churg (1975) found that lung cancer cases had more coated fibers in their lungs, even though only one case had known occupational exposure. The variations in percentage are probably from methodologic differences. In general, methods involving the counting of fibers/unit of weight or volume of lung tissue have greater associations with health outcomes in epidemiologic studies. However, coated fibers are not specific to asbestos (Gross et al, 1968) and cannot be related to asbestos unless the core has been identified as such by electron diffraction and/or x-ray analytical techniques (Pooley, 1970, 1975; Langer and Pooley, 1973, 1974; Fondimare et al, 1975).

Transmission electron microscopy has demonstrated the presence of chrysotile fibers or fibrils in the lungs of most consecutive autopsy cases in London (Pooley et al, 1970), New York (Langer et al, 1971) and Pittsburgh (Gross et al, 1973).

Although some differences in both the fibrotic and the carcinogenic

responses to asbestos fibers may depend on the type of fiber administered, all types have definitely shown both these kinds of action (eg, Karacharova et al (1979), Shin and Firminger (1973), Wagner et al (1976). Godwin and Jagatic (1970), Gross et al (1973), and Taskinen et al (1973) reported finding fibers in lymph nodes and in the spleen, abdomen, and intestinal mucosa of occupationally exposed patients with mesotheliomas and pleural nodules. These findings emphasize the practical importance of penetration and transport of the small fibers of asbestos from their initial sites of impaction. They also stress the importance of guarding against the entrance of asbestos fibers into the body by any route.

REFERENCES FOR CHAPTER III

1. Hendry NW (1965): The geology, occurrences, and major uses of asbestos. Ann N Y Acad Sci 132:1-766

2. Hueper WC (1966): Occupational and environmental cancers of the respiratory system, in, Rentchnick P (ed): Recent Results in Cancer Research, 3, New York, Springer-Verlag, 1966, p 38

3. 1970 Report of the Departmental Committee on Compensation for Industrial Diseases. C.D. 3495, 3496, London. Her Majesty's Stationery Office

4. Hoffman FL (1918): Mortality from respiratory diseases industry trades (Inorganic Dust), bulletin 231. US Dept of Labor, Bureau of Labor Statistics, 1918, pp 176-80

5. Pancoast HK, Miller TG, Landis HRM (1917): A roentgenologic study of the effects of dust inhalation upon the lungs. Trans Assoc Am Physicians 32:97-108

6. Cooke WE (1927): Pulmonary asbestosis. Br Med J 2:1024-25

7. McDonald S (1927): Histology of pulmonary asbestosis. Br Med J 2:1025-26

8. Mills RG (1930): Pulmonary asbestosis; Report of a case. Minn Med 130:495-99

9. Lynch KM, Smith WA (1930): Asbestosis bodies in sputum and lung. JAMA 95:659-61

10. Merewether ERA, Price CW (1930): Report on the effects of asbestos dust on the lungs and dust suppression in the asbestos industry. London, Her Majesty's Stationery Office

11. Merewether ERA (1934): A memorandum on asbestosis. Tubercle, 75:69-81, 109-118, 152-59

12. Fulton WB, Dooley A, Matthews JL, Houtz RL (1935): Asbestosis Part II: The nature and amount of dust encountered in asbestos fabricating plants. Part III: The effects of exposure to dust encountered in asbestos fabrication plants on the health of a group of workers. bulletin 42. Harrisburg, Pennsylvania Dept of Labor and Industry

13. Dreessen WC, Dallavalle JM, Edwards TL, Miller JW, Sayers RR (1938): A study of asbestosis in the asbestos textile industry. Public Health bulletin 241. US Treasury Dept, Public Health Service

14. Harries PG (1968): Asbestos hazards in naval dockyard. Ann Occup Hyg 11:135-45

15. Murphy RLH, Ferris GC Jr, Burgess WA, Worcester J, Gaensler EA (1971): Effects of low concentrations of asbestos, N Engl J Med 285:1271

16. Murphy RL, Levine BW, AlBazzaz FJ, Lynch JJ, Burgess WA (1971): Floor tile installation as a source of asbestos exposure. Am Rev Resp Dis 104:576-80

17. Lorimer WV, Rohl AN, Miller A, Nicholson WJ, Selikoff IJ (1976): Asbestos exposure of brake repair workers in the United States. New York Environmental Science Laboratory, Mount Sinai School of Medicine of the City University of New York, (in press)

18. Meurman LO, Kiviluoto R, Hakama M (1973): Mortality of employees of anthophyllite asbestos mines in Finland, in Bogovski P Gilson JC, Timbrell V, Wagner JC (eds): Proceedings of the Conference of Biological Effects of Asbestos. Lyon, pp 199

19. Weill H, Ziskind MM, Waggenspack C, Rossiter CE (1975): Lung function of consequences of dust exposure in asbestos cement manufacturing plants. Arch Environ Health 30:88-97, 1975

20. Ayer H, Burg J (1976): Cumulative asbestos exposure and forced vital capacity. Arch Environ Health (in press)

21. Selikoff IJ (1976a): Asbestos disease in the United States, 1918-1975. New York Environmental Science Laboratory, Mount Sinai School of Medicine of the City University of New York, (in press)

22. Anderson HA, Lilis R, Daum SM, Fischbein AS, Selikoff IJ (1976): Household-contact asbestos neoplastic risk. Ann NY Acad Sci 271:311-323

23. Wagoner JK, Johnson WM, Lemen RA (1973): Malignant and nonmalignant respiratory disease mortality patterns among asbestos production workers. Congressional Record-Senate Proceedings and Debates, 93rd Congress, First Session. US Govt Printing Office, Vol 119-Part 6, pp 7828-7830, March 14, 1973

24. Newhouse ML (1969): A study of the mortality of workers in an asbestos factory. Br J Ind Med 26:294

25. Enterline PE, Henderson V (1973): Type of asbestos and respriatory cancers in the asbestos industry. Arch Environ Health 27:312

26. Personal correspondence from Ronald M. Heymann, Commissioner, Department of Labor and Industry, State of New Jersey, July 21, 1971

27. Personal correspondence from Charles Serraino, Commissioner, Department of Labor and Industry, State of New Jersey, September 10, 1970

28. Selikoff IJ (1976): Asbestos disease in the United States 1918-1975. Presented at the Conference on Asbestos Disease, Rouen, France, October 27, 1975

29. Lynch KM, Smith WA (1935): Pulmonary asbestosis: Carcinoma of the lung in asbestos-silicosis. Am J Cancer 24:56

30. Gloyne SR (1935): Two cases of squamous carcinoma of the lung occurring in asbestosid. Tubercle 17:5

31. Wedler HW (1943b): Asbestose und lungenkrebs bei asbestose. Dtsch Arch Klin Med 191:189

32. Wedler HW (1943b): Asbestose und lungenkrebs. Dtsch Med Wochenschr 69:575

33. Wyers H (1946): That legislative measures have proved generally effective in the control of asbestosis. Glasgow, M.D. Thesis University of Glasgow, UK

34. Doll R (1955): Mortality from lung cancer in asbestos workers. Br J Ind Med 12:81

35. Mancuso TF, Coulter EJ (1963): Methodology in industrial health studies. The cohort approach with special reference to an asbestos company. Arch Environ Health 6:36-52

36. Selikoff IJ, Churg J, Hammond EC (1964): Asbestos exposure and neoplasia. JAMA 188:22

37. _____(1965):UICC working group on asbestos cancers. Arch Environ Health 11:221-29

38. Bohlig H, Dabbert AF, Palguen P, Hain E, Hinz I (1970): Epidemiology of malignant mesothelioma in Hamburg. Environ Res 3:365

39. Selikoff IJ (1970): Partnership for prevention - The insulation industry hygiene research program. Ind Med 39:4

40. Elmes PC, Simpson MJC (1971): Insulation workers in Belfast. 3. Mortality 1940-66. Br J Ind Med 28:226

41. Stumphius J (1971): Epidemiology of mesothelioma on Waicheren Island. Br J Ind Med 28:59

42. Rubion GF, Scansetti G, Conna A, Palestro G (1972): Epidemiology of pleural mesothelioma in North-Western Italy (Piedmont). Br J Ind 29:436

43. Selikoff IJ, Hammond EC, Seidman H (1973): Cancer risk of insulation workers in the United States, in Bogovski P, Gilson JC, Timbrell V, Wagner, JC (eds): Proceedings of the Conference of Biological Effects of Asbestos. Lyon, 1973, pp 209

44. Haries PG (1976): Experience with asbestos disease and its control in Great Britain's naval dockyards. Environ Res 11:261-267

45. Edge JR (1976): Asbestos related disease in Barrow-in-Furness. Environ Res 11:244-47

46. Cooper CW (1975): Study of sheet metal workers final contract report contract no. HSM-099-71-55 for National Institute of Occupational Safety and Health

47. Webster I (1973): Asbestos and malignancy. S Afr Med J 47:165

48. DeLajarte M, DeLajarte AY, Michand JL (1973): Mesothelioma pleuraux diffus. Etude preliminaire sur. 31 cas openes and rev. Fr Mal Resp 1: 697

49. Gobbato F, Ferri R (1973): Ricerca epidemiologica sull' incidenza del mesotelioma della pleura nella provincia di trieste. Lavoro Limano 25: 161

50. Greenberg M, Lloyd Davies TA (1974): Mesothelioma register 1967-68. Br J Ind Med 31:91

51. Hain E, Dalquen P, Bohlig H (1974): Katamnestische untersuchungen zur genese des mesotheliomas. Int Arch Arbeitsmed 33:15

52. Nurminen, Markku (1975): The epidemiologic relationship between pleural mesothelioma and asbestos exposure, Scan J Work Environ Health 1:128137

53. Sturm W (1975): Bericht uber die x. mesothelium. Konferenz vom III bis, 5: Mai 1974. Wien Z Ges Hyg 21:254-57

54. Zielhuis RL, Versteeg, JPJ, Planteijdt HT (1975): Pleura mesothelioma and exposure to asbestos. Int Arch Occup Environ Health 36:1-18

55. McDonald AD, Magner D, Eyssen G (1973): Primary malignant mesothelial tumors in Canada, 1960-1968. Cancer 31:869

56. McCaughey WTE, Oldham PD (1973): Diffuse mesotheliomas: Morbid anatomical and histological diagnostic criteria including observer

Mesothelial tumors in Canada, 1960-1968. Cancer 31:869

variation in histological diagnosis, in Bogovski P, Gilson JC, Timbrell V, Wagner JC (eds): Proceedings of the Conference on Biological Effects of Asbestos. Lyon, 1973, pp 58

57. Newhouse ML, Berry G, Wagner JC, Turok ME (1972): A study of the mortality of female asbestos workers. Br J Ind Med 29:134

58. Gilson JC (1973): Asbestos cancer: Past and future hazards. Proc R Soc Med 66:395

59. Hammond EC, Selikoff IJ (1973): Relation of cigarette smoking to risk of death of asbestos-associated disease among insulation workers in the United States, in Bogovski P, Gilson JC, Timbrell V, Wagner JC (eds): Proceedings of the Conference on Biological Effects of Asbestos. Lyon, 1973, pp 312

60. Selikoff IJ (1976b): Asbestos disease in the United States 1918-1975. Presented at the Conference on Asbestos Disease, Rouen, France, October 27, 1975.

61. Newhouse ML, Berry G (1975): The risk of developing mesothelial tumors among workers in an asbestos textile factory. Presented at the XVIII International Congress on Occupational Health. Brighton, England, 14-19 Sept.

62. Wagner JC (1960): Diffuse pleural mesothelioma and asbestos exposure in the Northwestern Cape Province. Br J Ind Med 17:260-71

63. Harrington JS, Gibson JC, Wagner JC (1971): Asbestos and mesothelioma in man. Nature (L) 232:54

64. Webster I (1973): Malignant pleural mesothelioma in an asbestos worker. Med J Aust 49:952

65. McNulty JC (1962): Malignant pleural mesothelioma in an asbestos worker. S Afr Med J 47:165

66. Jones JFP, Pooley FD, Smith PG (1976): Factory populations exposed to crocidolite asbestos. A continuing survey IARC regist. meeting, (in press)

67. McDonald JC (1973): Asbestosis in Chrysotile mines and mills, in Bogovski P, Gilson JC, Timbrell V, Wagner JC, (eds): Proceedings of the Conference on Biological Effects of Asbestos. Lyon, 1973, pp 312

68. McDonald JC, Becklake MR, Gibbs GW, McDonald AD, Rossiter CE (1974): The health of chrysotile asbestos mine and mill workers of Quebec. Arch Environ Health 28:61

69. McDonald AD, McDonald JC (1976): Epidemiologic studies of the illnesses due to asbestos in Canada. Rev Fr Mal Resp 4:25 (Supp 2)

70. Kogan FM, Guselnikova NA, Gulevskaya MR (1972): The cancer mortality rate among workers in the asbestos industry of the Urals. Gig Sanit 37:29

71. Enterline PE, Henderson V (1973): Type of asbestos and respiratory cancer in the asbestos industry. Arch Environ Health 27:312

72. Borow M, Conston A, Livernese L, Schalet N (1973): Mesothelioma following exposure to asbestos: A review of 72 cases. Chest 64:641-46

73. Gillam JD, Dement JM, Lemen RA, Wagoner JK, Archer VE, Blejer HP (1976): Mortality patterns among hard rock gold miners exposed to an asbestiform mineral. Ann NY Acad Sci 271:345-352

74. Seidman H, Lilis R, Selikoff I (1976): Short-term asbestos exposure and delayed cancer risk. Third International Symposium Detect. Prevent. Cancer, New York, 26, April - 1 May, 1976

75. Meurman L, Kiviluoto R, Hakama M (1974): Mortality and morbidity among the working population of anthophyllite asbestos miners in Finland. Br J Ind Med 31:105

76. Kiviluoto R (1960): Pleural calcification as a roentgenologic sign of nonoccupational endemic anthophyllite-asbestosis. Acta Radiol Suppl 195:1

77. Meurman L (1966): Asbestos bodies and pleural plaques in a Finnish series of autopsy cases. Acta Pathol Microbiol Scand Suppl 181:1

78. Selikoff IJ (1974): Epidemiology of gastrointestinal cancer. Environ Health Pers 9:299

79. Mancuso TF, EL Attar AA (1967): Mortality pattern in a cohort of asbestos workers. A study based on employment experience. J Occup Med 9:147

80. Newhouse ML (1973): Cancer among workers in the asbestos textile industry, in Bogovski P, Gilson JC, Timbrell V, Wagner JC (eds): Proceedings of the Conference on Biological Effects of Asbestos. Lyon, pp 203

81. McDonald JC, Becklake MR, Gibbs GW, McDonald AD, Rossiter CE (1974): The health of chrysotile asbestos mine and mill workers of Quebec. Arch Environ Health 28:61

82. Schneiderman MA (1974): Digestive system cancer among persons subjected to occupational inhalation of asbestos particles: A literature review with emphasis on dose response. Environ Health Pers 9:307

subjected to occupational inhalation of asbestos

83. Stell PM, McGill T (1973): Asbestos and laryngeal carcinoma. Lancet 2:416

84. Morgan RW, Shettigara PT (1976): Occupational asbestos exposure, smoking, and laryngeal carcinoma. Ann N Y Acad Sci 271:308-310

85. Newhouse ML, Berry G (1973): Asbestos and laryngeal carcinoma. Lancet 2:615

86. Anderson HA, Lilis R, Daum SM, Fischbein AS, Selikoff IJ (1976): Householdcontact asbestos neoplastic risk. Ann N Y Acad Sci 271:311,23

87. Wagner JC, Sleggs CA, Marchand P (1960): Diffuse pleural mesothelima and asbestos exposure in the North-Western Cape Province. Br J Ind Med 17:260

88. Newhouse ML, Thompson H (1966): Mesothelioma of pleura and peritoneum following exposure to asbestos in the London area. Br J Ind Med 22:261

89. Bohlig H, Hain E (1973): Cancer in relation to environmental exposure, type of fibre, dose, occupation and duration of exposure, in Bogovski P, Gilson JC, Timbrell V, Wagner JC, (eds): Proceedings of the Conference on Biological Effects of Asbestos. Lyon, 1973, pp 217

90. Gilson JC (1970): Asbestos health hazards. Recent observations in the United Kingdom, in Shapiro HA (ed): Pneumoconiosis. Proceedings of the International Conference, Johannesburg, Cape Town, Oxford University Press, 1970, pp 173

91. Greenberg M, Lloyd Davies TA (1974): Mesothelioma register 1967-1968. Br J Ind Med 31:91

92. Selikoff IJ, Hammond EC, Churg J (1968): Asbestos exposure, smoking and neoplasis. JAMA 204:106

93. Doll R (1971): The age distribution of cancer: Implications for models of carcinogenesis. J R Stat Soc A 134:133

94. Berry G, Newhouse ML, Turok M (1972): Combined effects of asbestos exposure and smoking on mortality from lung cancer in factory workers. Lancet 2:476

95. Hammond EC, Selikoff IJ (1973): Relation of cigarette smoking to risk of death of asbestos-associated disease among insulation workers in the United States, in Bogovski P, Gilson KC, Wagner KC (eds): Proceedings of the Conference on Biological Effects of Asbestos. Lyon, 1973, pp 312

96. Lemen RA (1976): Lung cancer in female asbestos workers. Letter to Vernon Rose, Director, Division of Criteria Documentation and Standards Development

97. Timbrell V (1965): The inhalation of fibrous dusts. Ann NY Acad Sci 132:255

98. Timbrell V (1972a): Alignment of amphibole asbestos fibres by magnetic fields. Microscopy 20:365

99. Timbrell V, Griffiths DM, Polly FD (1971): Possible biological importance of fibre diameters of South Africa amphiboles. Nature (London) 232:55

100. Timbrell V, Rendall REG (1972b): Preparation of the UICC standard reference samples of asbestos. Powder Technol 5:279

101. Sebastian P, Fondimare A, Bignon J, Moncheax G, Desbordes J (1975): Topographic distribution of asbestos fibers in human lungs in relation to occupational and nonoccupational exposure. Presented at the Symposium on Particles and Vapors at Edinburgh, Scotland. September 1975

102. Ascroft T, Heppleston AG (1973): The optical and electron microscope determination of pulmonary asbestos fibre concentration and its relation to the human pathological reaction. J Clin Pathol 26:224

103. Pooley FD (1972): Asbestos bodies, their formulations, composition and character. Environ Res 5:363-79

104. Pooley FD (1973): Mesothelioma in relation to exposure, in Bogovski P, Gilson JC, Timbrell V, Wagner JC (eds): Proceedings of the Conference on Biological Effects of Asbestos. Lyon, 1973, pp 99

105. Fondimare A. Desbordes J, Perrotey J (1974): Etude semi quantitative de l'empoussierage par l'amiante dans 14, Arch Anat Pathol, (Paris) 22:55

106. Le Bouffant L, Martin JC, Brueres S, Tichoux G, Normand C (1976): Quelques observations sur les siches d'amiante et formations anormalles rencontrees dans les poumons asbestosiques, lapathologie de l'amiante symposium 27-28 Oct. 1975, Rouen, France

107. Gross P, de Treville RTP, Haller MN (1969): Pulmonary ferruginous bodies in city dweller. A study of their central river. Arch Environ Health 19:186

108. Bignon J, Goni J (1969): Pulmonary ferruginous bodies in France. Am Rev Resp Dis 101:804

109. Selikoff IJ, Hammond EC, Churg J (1972): Carcinogenicity of amosite asbestos, Arch Environ Health 25:183

110. Thomson JG, Gross P (1973): Are ferruginous bodies an indication of atmospheric pollution by asbestos? in Bogovski P, Gilson JC, Trimbrell V, Wagner JC (eds): Proceedings of the Conference on Biological Effects of Asbestos. Lyon, 1973, pp 238

111. Davis JMG, Gross P (1973): Are ferruginous bodies an indication of atmospheric pollution by asbestos?, in Bogovski P, Gilson JC, Timbrell V, Wagner JC (eds): Proceedings of the Conference on Biological Effects of Asbestos. Lyon, 1973, pp 238

112. Oldham PD (1973): A trial of techniques for counting asbestos bodies in tissue, in Bogovski P, Gilson JC, Timbrell V, Wagner JC (eds): Proceedings of the Conference on Biological Effects of Asbestos. Lyon, 1973, pp 45

113. Meurman LO (1968): Pleural fibrocalcific plaques and asbestos exposure. Environ Res 2:30

114. Doniach I, Swettenham KV, Hathorn MKS (1975): Prevalence of asbestos bodies in a necropsy series in East London: Association with disease, occupation and domiciliary address. Br J Ind Med 32:16-30

115. Warnock ML, Churg AM (1975): Association of asbestos and bronchogenic carcinoma in a popuation with low asbestos exposure. Cancer 35:1236-42

116. Gross P, de Treville TP, Cralley J, Davis JMG (1968): Pulmonary ferruginous bodies. Arch Pathol 85:538-46

117. Pooley F, Oldham P, Um Chang-Hynn, Wagner JC (1970): The detection of asbestos in tissues, in, HA Shajsiro (ed): Pneumoconiosis, Proceedings International Conference Johannesburg, Capetown, Oxford, University Press, 1969, 108 pp

118. Pooley FD (1975): The identification of asbestos dust with an electron microscope micro-probe analyses. Ann Occup Hyg 18:181-86, 1975 (in press)

119. Langer AM, Pooley FD (1973): Identification of single asbestos fibres in human tissues, in Bogovski P, Gilson JC, Timbrell V, Wagner JC (eds). Proceedings of the Conference on Biological Effects of Asbestos. Lyon, 1973, pp 119

120. Langer AM. Mackler AD, Pooley FD (1974): Electronmicroscopical investigation of asbestos fibres. Environ Health Pers 9:63

121. Langer AM, Selikoff IJ, Sastre A (1971): Chrysotile asbestos in the lungs of persons in N.Y. City. Arch Environ Health 22:348-361

122. Gross P (1974): Is short-fibered asbestos dust a biological hazard? Arch Environ Health 29:115-117

123. Karacharova VN, Ol'shvang RA, Kogan FM (1969): Changes in certain organs after experimental introperitoneal injection of asbestos-containing dusts. Byull Eksp Biol Med 67:117-120

124. Shin ML, Firminger HI (1973): Acute and chronic effects of introperitoneal injection of two types of asbestos in rats with a study of the histopathogenesis and ultra structure of resulting mesothelioma. Am J Pathol 70:291-314

125. Godwin MC, Jagatic J (1970): Asbestos and mesotheliomas. Environ Res 3:391-416

126. Gross P, Davis JMG, Harley RA, deTreville RTP (1973): Lymphatic transport of fibrous dust from the lungs. J Occup Med 15:186-189

127. Taskinen E, Ahlman K, Wiideri M (1973): A Current Hypothesis of the lymphatic transport of inspired dust to the parietal pleura. Chest 64:193-196

TABLE III-1

STUDIES OF HUMAN POPULATIONS-NONMALIGNANT RESPIRATORY DISEASE

Author	Date	Finding	Group and Exposure
Historical Studies			
Murray	1906	First reported case of asbestosis	Asbestos workers
Cooke	1927	Case of asbestosis reported	"
McDonald	1927	Two cases of asbestosis reported	"
Mills	1930	First case of asbestosis reported in U.S.	"
Lynch and Smith	1930	Ferruginous or "asbestosis bodies" found in sputum	"
Epidemiological Studies			
Murphy	1971	Asbestosis	Pipe insulators
Lorimer et al	1976	X-ray abnormalities consistent with with asbestosis and restrictive pulmonary function testing	Brake repair maintenance workers
Meurman et al	1973	Dyspnea and cough	Asbestos workers
Weill et al	1975	Decreased lung function	Asbestos cement manufacturing workers
Ayer and Burg	1976	Decrease in pulmonary function	Asbestos textile workers with less than 10 yr exposure
Selikoff	1976a	Asbestosis	Former insulation plant employees with as little as one day exposure
Anderson et al	1976	X-rays consistent with asbestosis	Household and family members of asbestos worker
Wagner et al	1973	Death due to nonmalignant respiratory disease and diseases of heart, in part secondary to pulmonary disease	Chrysotile workers
Newhouse	1969	Death due to nonmalignant respiratory disease	Male asbestos textile and insulation workers
Enterline and Henderson	1973	Death due to asbestosis	Asbestos plant workers
Selikoff	1976a	"	Insulation workers and factory workers exposed to asbestos
Bohs	1968	X-ray evidence of asbestos	Workers in asbestos industry in Britain after 1933 with perponderance of less than 20 yr exposure
Lewinsohn	1972	X-ray abnormalities	Asbestos workers in Britian
Gillam et al	1976	Nonmalignant respiratory disease	Amosite miners

TABLE III-2

STUDIES OF HUMAN POPULATION CARCINOGENICITY

Author	Date	Finding	Group and Exposure
Occupational Exposure			
Historical Studies			
Lynch and Smith	1935	Suspicion of association	Asbestos workers
Gloyne	1935	Between asbestos and lung cancer	"
Wedler	1943a,b	Case reports of pleural and peritoneal tumors associated to asbestos	"
Doll	1955	Lung cancer	Asbestos textile workers employed before 1930
Mancusco and Coulter	1963	Lung cancer and mesotheliomas	Asbestos workers
Selikoff	1964	"	"
Epidemiological Studies			
Lung, Pleural and Peritoneum			
Mixed Types of Fibers			
Newhouse (UK)	1969	Bronchial cancer, pleural and peritoneal mesotheliomas	Asbestos manufacturing, insulation and shipyard workers
Bohlig et al (FRG)	1970	"	"
Selikoff et al (USA)	1970	"	"
Elmes and Simpson (UK)	1971	"	"
Stumphius (Netherlands)	1971	"	"
Rubino et al (Italy)	1972	"	"
Selikoff et al	1973	Lung cancer	Insulation workers, chrysotile and amosite asbestos exposure
Enterline and Henderson	1973	Respiratory cancer	Retired production and maintenance workers in asbestos industry
Harries	1976	Mesotheliomas	Naval dockyard workers
Edge	1976	Carcinoma of bronchus	Shipyard workers

TABLE III-2 (CONTINUED)

STUDIES OF HUMAN POPULATION CARCINOGENICITY

Author	Date	Finding	Group and Exposure
Mixed Types of Fibers			
DeLajarte et al (France)	1973	Evidence of association between mesotheliomas and past exposure to asbestos	Occupational exposures in some cases as brief as one day
Gobbato and Ferri (Italy)	1973	"	"
Webster (South Africa)	1973	"	"
Greenberg and Lloyd Davies (UK)	1974	"	"
Hain et al (Fed. Rep. Germany)	1974	"	"
Nurminen (Finland)	1975	"	"
Stunn (Ger. Dem. Rep.)	1975	"	"
Zielhuis (The Netherlands)	1975	"	"
Newhouse et al	1973	Peritoneal tumors associated to heavy exposures	"
Gilson	1973	5% to 7% asbestos workers' deaths due to mesotheliomas	"
Hammond and Selikoff	1973		"
Selikoff	1976	"	"
Newhouse and Berry	1975	11% asbestos workers deaths due to mesotheliomas	"
Single Types of Fibers			
Crocidolite			
Wagner	1960	Pleural and peritoneal cancer	Workers in mines, mills and in transportation and handling of crocidolite and population in vicinity of mines
Harrington et al	1971	Mesotheliomas	Mining population of crocidolite mines
Webster	1973		
McNulty	1962	"	Miners of crocidolite
Jones et al	1976	"	Women working with crocidolite in WWII gas mask canister factories

TABLE III-2 (CONTINUED)

STUDIES OF HUMAN POPULATION CARCINOGENICITY

Author	Date	Finding	Group and Exposure
Chrysotile			
McDonald et al	1973,1974	Lung cancer	Chrysotile mine and mill workers
Kogan et al	1972	Total cancer Lung cancer	Workers in asbestos mining and milling, men and women
Wagoner et al	1973	Respiratory cancer	Workers in manufacturing of textile, friction and packaging products using chrysotile
Enterline and Henderson	1973	"	Men 65 yr and older, retired production or maintenance employees in asbestos industry exposed only to chrysotile
Borow et al	1973	Mesotheliomas	Workers at plant using chrysotile, all ages
Amosite			
Gilliam et al	1976	Malignant respiratory disease	Miners exposed to amphibole fibers in cummingtonite-grunerite ore series
Selikoff et al	1976a,b	Mesotheliomas, lung cancer	Insulation workers in factory using amosite
Anthophyllite			
Neurman et al	1974	Bronchial cancer, dyspnea and cough	Anthophyllite mining employees
Other Cancer			
Mancuso and El Attar	1967	Cancer of gastrointestinal tract	Asbestos workers
Elmes and Simpson	1971	"	"
Kogan et al	1972	"	"
Newhouse	1973	"	"
Wagoner et al	1973	"	"
McDonald et al	1974	"	"
Selikoff et al	1974	"	"
Stell and McGill Morgan et al	1973 1976	Squamous carcinoma of larynx	Workers with exposure to asbestos
Newhouse and Perry	1973	Cancer of larynx	Asbestos workers

TABLE III-2 (CONTINUED)

STUDIES OF HUMAN POPULATION CARCINOGENICITY

Author	Date	Finding	Group and Exposure
Nonoccupational Exposure			
Anderson et al	1975	Mesotheliomas	Family members of asbestos workers
Wagner et al Newhouse and Thompson Bohlig and Hain	1960 1965 1973	"	Individuals in neighborhood of industrial sources of asbestos
Gilson Greenburg and Lloyd Davies	1970 1974	"	New cases from areas with recognized industrial source of asbestos
Kiviluoto	1960	Pleural plaques	Persons in farming region of Bulgaria where minute quantities of anthophyllite, tremolite and sepiolite in soil and non-occupationally exposed persons in anthophyllite mining area of Finland
Other Studies			
Newhouse Newhouse et al	1969- 1972	Cancer, mesothelioma "	Women factory workers exposed to chrysotile, amosite and crocidolite
Howard et al	1976	Lung cancer	Workers in asbestos industry from 1933 to 1950 and after 1950
Cooper et al	1975	"	Sheet metal workers with 5 or more years exposure

IV. SAMPLING METHODS AND ENVIRONMENTAL DATA

Review of Sampling and Analysis Techniques for Asbestos

A variety of sampling and analysis techniques have been used to identify asbestos fibers and determine their concentrations in air, water, mineral samples, and biologic tissue. These include optical and electron microscopy, x-ray diffraction, and differential thermal analysis. Asbestos fiber identification and quantitation in occupational and environmental air samples is difficult for a variety of reasons:

1) Asbestos fibers are generally present in low mass quantities even though fiber number concentrations may be high.

2) Many instrumental analytical techniques cannot differentiate asbestos fibers from their nonfibrous mineralogic polymorphs.

3) Many airborne asbestos fibers are generally below resolution limits of the optical microscope. These fibers may only be detected by using electron microscopic methods.

4) For identification of the various asbestos fiber types by electron microscopy, electron diffraction and microchemical analyses must be performed which require expensive instrumentation and analysis time.

(a) Electron Microscopy and Microchemical Analysis

Both transmission and scanning electron microscopy have been used for asbestos fiber identification and quantitation. In addition to morphologic observation, selected area electron diffraction and microchemical

analytical techniques may be used for fiber identification.

In addition to superior resolution capabilities, most modern transmission electron microscopes are equipped with electron diffraction facilities. Crystalline materials scatter electrons in regular patterns related to their crystal structure. The image of the scattered electrons is mainly predicted by Bragg geometry. In the transmission electron microscope, the diffraction image is formed in the back focal plane of the objective lens and is focused in the viewing screen by defocusing the intermediate lens. Visual observation of single fiber (single crystal) electron diffraction patterns may be used to differentiate chrysotile fibers from amphibole fibers (Langer et al, 1974; Timbrell 1970). Chrysotile fibers produce streaked diffraction patterns (lattice defects), with the streaks or layer lines nearly perpendicular to the fiber length. The spacing between the layer lines denotes the fiber "a" axis of approximately 5.3 $\mathring{A}$. Reflections along the layer lines are usually very streaked and Debye-Scherrer rings are common. With progressive electron beam bombardment, the diffraction pattern may change because of fiber damage. The "central core" of chrysotile fibers may also aid in fiber identification with the precaution that the central core is not always discernable and may disappear with the beam damage (Langer et al, 1974). Also, other fibrous minerals may have hollow cores.

The amphibole minerals are generally straighter in appearance than chrysotile fibers. Moreover, light and dark banding (diffraction images) may cross the fiber at right angles (Langer et al, 1974). Diffraction contrast figures have been observed on all amphibole fiber types. Selected area diffraction patterns for the amphibole asbestos minerals are all

similar in appearance; therefore, visual observation of these patterns is sufficient only to classify the fiber as being a fibrous amphibole (Langer et al, 1974; Cook et al, 1974). Amphibole electron diffraction patterns show layers and sometimes streaks perpendicular to the fiber length with the spacing between the layer lines or streaks representing the fiber "c" axis (Langer et al, 1974) of approximately 5.3 Å. In contrast to chrysotile, less streaking along the layer lines is observed with the spot repeat along the lines representing one of the two remaining lattice spacings ("b" or "a") depending on fiber orientation relative to the electron beam. Typically, approximately 30 seconds is needed to perform a selected area electron diffraction analysis on a single fiber.

In addition to visual observation of electron diffraction patterns for fiber identification, photographs can be made of the diffraction patterns and crystal "d" spacings measured from the plate and calculated using the instrument camera constant (Timbrell, 1970). Both "spot" and polycrystalline patterns may be measured. It must be borne in mind that intensities may not be the same as those observed for x-ray powder patterns and additional reflections may be present.

Electron beam microchemical analytical techniques may sometimes be used to identify asbestos fibers from other fibrous particles (Rubin and Maggiore, 1974; Ferrell et al, 1975; Langer et al, 1975; Maggiore and Rubin, 1973). The most common system presently in use is the energy dispersive x-ray detector in combination with a scanning or transmission electron microscope. Wavelength x-ray analyzers and the conventional electron microprobe have been used; however, their routine application is limited because of data acquisition times (Langer et al, 1975). On the

other hand, data acquisition times with energy dispersive analyzers are far less, ranging from 20 to 80 seconds/analysis.

Semiquantitative microchemical analysis in the electron microscope is based on the fact that a beam of high energy electrons incident on an asbestos fiber generates x-rays characteristic of the elements present in that fiber. The generated x-rays are observed by means of a detector (lithium-drifted silicon crystal) placed in the electron microscope column close to the specimen. The energy of the x-ray photon is converted to a voltage pulse which is amplified, digitized and stored in a multichannel analyzer or a minicomputer. The content of the memory is usually displayed on a CRT (Maggiore and Rubin, 1973). With the energy dispersive detector, all elements with atomic numbers of sodium or higher may be analyzed. Continuous background or brehmsstrahlung radiation is always present with the x-ray spectrum.

Each of the asbestos minerals has an x-ray spectrum which is usually characteristic enough, when combined with fiber morphology, to allow its identification (Rubin and Maggiore, 1974; Ferrell et al, 1975; Dement et al, 1975). Visual observation of the semiquantitative fiber x-ray spectra is usually sufficient for fiber identification; however, three component diagrams have been used after subtracting the continuous background from the semiquantitative x-ray spectrum (Ferrell et al, 1975). For asbestos fiber analysis, matrix corrections are rarely used. Typically, iron, magnesium, and silicon are plotted on the three component diagram and compositional boundaries for the asbestos minerals established. This technique suffers from inability to use all compositional data obtained, such as presence or absence of sodium, calcium, aluminum and manganese, which aid in identification.

technique suffers from inability to use all compositional data obtained

With energy dispersive x-ray techniques, possession of proper elemental intensities may not be sufficient for positive identification as many fibrous minerals show similar elemental intensities. For example, chrysotile, anthophyllite, and fibrous talc, which have similar elemental compositions, may be difficult to differentiate. However, these materials may easily be distinguished by using selected area electron diffraction. In addition, unique identification of the various fibrous amphiboles usually requires both selected area diffraction and microchemical analysis. Transmission electron microscopes equipped with an energy dispersive x-ray detector are now available which allow simultaneous observation of morphology, crystal structure, and elemental composition. These microscopy systems have been used to study asbestos fibers in environmental and material samples. (Cook et al, 1974; Dement et al, 1975)

Quantitative analysis of asbestos fiber concentrations in environmental and tissue samples has been accomplished by electron microscopy. Environmental samples (water and air) are generally collected by first concentrating the sample by filtration, centrifuging, etc (Cook et al, 1974; Nicholson, 1974). The filters (Millipore) and polycarbonate filters (Nuclepore) are prepared for electron microscopic analysis by various methods. For scanning electron microscopy, Nuclepore filters, because of their smooth surface, may be directly coated with an appropriate metal (gold, etc) and analyzed (Porter and Berggren, 1974). Millipore filters have a rough surface texture and are not generally suitable for direct coating for scanning electron microscopy as small fibers may escape detection due to impaction below the filter surface (Nicolson, 1974).

For transmission electron microscopy, the filter substrate must be removed and the particles mounted on suitable electron microscopy grids. A wide variety of mounting techniques have been used. The two most commonly used methods are the Jaffe Wick and condensation washing techniques. The techniques offer simplicity in addition to maintaining the original particle size distribution of the sample. Different investigators have reported particle losses up to 60% with Millipore filters while using the condensation washing method with rapid filter dissolution, whereas losses with the Jaffe Wick method have been reported to be considerably less (>10%) (Beaman and File, 1975). Lesser particle loss has been observed with the condensation washing method when longer times for dissolution of the filter are used. Ortiz and Loom (1974) reported that a modification of the Jaffe Wick method, whereby the filter is first coated with silicon monoxide and carbon by vacuum evaporation prior to dissolving the Millipore filter, minimized particle loss. Several investigators have reported minimal particle loss with Nuclepore filters when the filter is first carbon-coated prior to dissolving the filter substrate (Cook et al, 1974; Maggiore and Rubin, 1973).

In addition to the so-called direct clearing/mounting techniques mentioned above, many other techniques have also been used for preparing environmental samples. Seikoff et al (1972) have used a so-called "rub-out" technique whereby the Millipore filter is ashed in a low temperature asher to remove organic or carbonaceous material. The residue is then dispersed on a microscope slide using a solution of 1% Nitrocellulose in amyl acetate. After grinding with a watch glass to liberate individual fibers, the sample is dispersed evenly between two microscope slides to

amyl acetate. After grinding with a watch glass to liberate individual

form a thin film which is transferred to standard electron microscope grids. Particle losses averaging 50% have been reported with this technique. This technique also increases the apparent number of fibers present due to breaking up of fiber bundles. Asbestos fiber levels in environmental samples and biologic tissue are usually expressed as asbestos fibers/unit volume of sample (fibers/m^3, fibers/liter, fibers/g dry lung, etc). These concentrations are determined by counting fibers within calibrated areas on the electron microscope viewing screen or counting fibers from photographs. Asbestos fiber concentrations in water samples determined by laboratories using the same mounting techniques have been reported to vary by a factor of 2-3 (Cook et al, 1974). Much larger variations have been reported between laboratories using different techniques.

Asbestos mass (chrysotile) concentrations in environmental samples have also been determined using electron microscopy. This is accomplished by measuring the length and diameter (volume) of each fiber and calculating the mass using the appropriate density (Selikoff et al, 1972). The accuracy of this technique has not been studied in detail.

Electron microscopic techniques represent the "best available" methods for asbestos fiber analysis. However, application of these techniques to routine samples is not practical because of extremely high analysis costs ($200-$400/sample), long analysis times, and limited equipment availability.

(b) X-Ray Diffraction

X-ray powder diffractometry is one of the standard mineralogic techniques used in the analysis of solid crystalline phases. X-ray

diffraction has been widely used for identification and quantitation of asbestos fibers in bulk materials such as talc (Stanley and Norwood, 1974; Rohl and Langer, 1974) and other industrial materials (Crable and Knott, 1968; Keenan and Lynch 1970).

X-ray diffraction has also been used to study amphibole asbestos contamination of water samples (Cook et al, 1974). X-ray diffraction is generally considered more sensitive for asbestos than light microscopy, although less sensitive than electron microscopy (Rohl and Langer, 1974).

Diffraction lines and relative intensities for each of the asbestos minerals have been published and may be found in the ASTM Powder Diffraction File. Variations in asbestos fiber chemical composition, especially for the amphiboles, may result in slight peak shifts from reported x-ray diffraction data.

Quantitative determinations of asbestos fiber levels in material samples (talc, etc) require that particle size first be reduced to an average of 0.1 - 10 μm. Preferred orientation and surface roughness must also be eliminated.

A number of techniques have been used to minimize preferred orientation effects including binder and slurry mounting methods, sifting and backloading of dry powders, and several others. To minimize preferred orientation, Rohl and Langer (1974) have developed a method for filtering an aqueous slurry through Millipore filters using a filtration adapter attached to a hypodermic syringe. Other investigators have used the backloading technique with multiple x-ray diffraction scans.

Using conventional scan rates (0.5 - 1 degree 2 theta/minute), lower limits of detection of asbestos by x-ray diffraction of 5% in bulk samples

have been reported (Crable and Knot, 1966). Automated step scanning procedures by which diagnostic reflections are slowly scanned and integrated counts recorded have been reported to significantly reduce detectable limits. Rohl and Langer (1974) have detected anthophyllite at 2.0%, chrysotile at 0.25%, and tremolite at 0.10% by wieght in a talc matrix using external dilution standards for calibration. Similar lower detectable levels have been reported by Stanley and Norwood (1974).

Application of x-ray diffraction for routine asbestos fiber analysis of environmental samples has been limited. Birks et al (1975) have reported a feasible study concerning quantitative analysis of airborne asbestos. Their technique involved alignment of the asbestos fibers in an electrostatic field to enhance diffraction intensity followed by x-ray counting in a specially designed diffraction apparatus with two x-ray detectors. A lower limit of detection of 0.4 - 0.5 μg was reported. This technique has not been applied to actual environmental samples.

Amphibole and cummingtonite-grunerite mass concentrations in water samples have been semiquantitatively determined using x-ray diffraction with step scanning (Cook et al, 1974). This technique involves filtering the water through 0.45-μm Millipore filters followed by step scanning a major amphibole diffraction peak (110) and a peak specific to cummingtonitegrunerite (310). The integrated peak count above background is recorded and mass concentrations are determined using external dilution standards.

Proper selection of diagnostic reflections to maximize detection sensitivity and minimize interference due to other mineral phases is necessary for proper use of x-ray diffraction. It must also be recognized

that x-ray diffraction methods are not capable of differentiating between asbestos fibers and their nonfibrous mineralogic polymorphs. This fact, combined with relatively poor detection levels, suggests that alternate techniques such as electron microscopy should be combined with x-ray analysis.

(c) Differential Thermal Analysis

Differential thermal analysis has been used to determine asbestos fiber levels in talc samples (Schlez, 1974) Chrysotile (serpentine minerals) shows a dehydroxylation endotherm at approximately 650 degrees C and an exotherm at approximately 820 degrees C, associated with the formation of forsterite. These peaks may be used for quantitative analysis. Using a 140-mg sample holder with an exposed loop differential thermcouple and a 10 degree C/minute heating rate, Schlez (1974) reported that a 1% concentration of chrysotile could be detected in pharmaceutical grade talc. A dynamic helium atmosphere was maintained to sweep out gaseous mineral decomposition products and to prevent oxidative reactions.

Differential thermal analysis has not been used for environmental samples as lower limits of mass detection are extremely poor. Differential thermal analysis, like x-ray diffraction, is not capable of differentiating between asbestos fibers and their nonfibrous mineralogic polymorphs.

(d) Optical Microscopy

A number of optical microscopic techniques have been used to identify and/or quantitate asbestos fibers in environmental samples. These include petrographic and phase contrast microscopy. Petrographic microscopic techniques may be used to identify asbestos fibers greater than approximately 0.2 - 0.3 μm in diameter. Using the polarizing microscope,

various optical crystallographic measurements such as refractive index, extinction angles, and sign of elongation may be measured and compared with data reported for standard asbestos reference samples. Typical optical data for selected asbestos minerals are shown in Table IV-1 (Julian and McCrone, 1970).

Dispersion staining with polarized light has been used to identify asbestos fibers, as reported by Julian and McCrone (1974). With this technique, the fibers are immersed in a mounting medium with a steeper dispersion curve than the fibers. A central or annular stop is used in the objective lens back focal plant to allow either the wavelength of light at which the index of the particle matches that of the mounting media, or complements to that color to reach the observer's eye. Using plane polarized light, asbestos fibers show two characteristic dispersion staining colors; one for the light vibration parallel to and the other for that perpendicular to the fiber length. The dispersion colors depend on the refractive index media in which the fibers are mounted, as shown in Table IV-2. Dispersion staining colors may change slightly depending on the geographic area from which the asbestos was mined and subsequent treatment. Fibers less than 0.5 μm in diameter may not be identified by this technique because of difficulties in distinguishing colors.

Phase contrast optical microscopy is the technique specified for determining the Occupational Safety and Health Administration asbestos standard (US Department of Labor 1975). The method consists of collecting breathing zone samples during 15-minute to 8-hour periods on membrane filters (millipore AA). Samples are analyzed by first clearing the membrane filter to make it optically transparent, then by fiber counts at

400-500X magnification by phase contrast optical microscopy. Asbestos fibers are defined as those particles with a length greater than 5 μm and a length-to-diameter ratio of 3:1, or greater. This technique, by which only fibers longer than 5 μm are counted, is recognized as only an index of total fiber exposure and does not imply that shorter fibers do not pose a health hazard. The relative proportion of airborne fibers longer than 5 μm has been shown by Dement et al (1975) to vary from 1 to approximately 50% depending on the industrial operation and asbestos fiber type. In addition to problems of detecting short fibers, phase contrast microscopy may not be specific for asbestos fibers in industrial operation where mixed fiber types are encountered.

Despite its limitations, phase contrast microscopy represents the only technique available that can reasonably be used for routine asbestos fiber sampling and analysis. It is adaptable to personal sampling where low air volumes are sampled and analysis equipment is readily available.

Minimum detectable fiber concentrations by phase contrast microscopy depend on a number of factors such as air volume sampled, microscope field counting area, number of microscopic fields counted, and presence or absence of nonfibrous particles. Theoretical minimum detectable concentrations may be calculated assuming one fiber longer than 5 μm is observed per 100 microscopic fields (after filter background subtraction). Table IV-3 shows theoretical minimum detectable fiber concentrations as a function of sample period for a typical microscope arrangement. For a 15-minute sampling period, 0.04 fibers >5 μm/cc may be detected; however, with an 8-hour sample, 0.001 fibers/cc can be detected. These minimum concentrations are similar to those reported by Corn and Sansone (1974).

These authors reported that 0.01 fibers/cc could be detected with a 2-hour sample period (40 microscopic fields counted).

The above calculations represent theoretical minimum detectable concentrations, not considering the many factors affecting precision and accuracy of the technique. There are many sources of variability in the laboratory analysis technique. The major sources of variability are as follows:

1) Variability of fiber distribution across the filter surface.
2) Variability of fiber distribution on a given filter wedge being analyzed.
3) Variability due to differences between microscopes.
4) Variability due to differences between individual counters.
5) Variability in laboratories.

Leidel and Busch (1974) found that the fiber distribution on a given filter section could best be described by the Poisson-distribution. However, Conway and Holland (1973) found that the distribution of fibers on filters was not uniform and were more disperse than predicted by the Poisson distribution, so that concentrations between sections could vary by as much as 50-60%. Similar results were found by Rajhans and Bragg (1975) in Series I of their study.

If the Poisson distribution is taken to adequately describe fiber distributions on filter sections, the standard deviation of the fiber count may be estimated from the square root of the count. In order to maintain an acceptable Coefficient of Variation (CV) (below 20%), a minimum of 25 fibers must be counted. For a typical industrial asbestos sample of 2

hours (2 lpm flow), this would correspond to a concentration of 0.13 fibers/cc.

The precision of the entire sampling and analysis procedure (all sources of variability) has been estimated by Leidel et al (1975). These authors estimated the total CV to be 22%.

Comparisons of Asbestos Mass Concentrations (ng/m^3) and Fiber Number Concentrations (fibers/cc)

In order to relate ambient asbestos levels, which are generally expressed as ng/m^3, to occupational exposures, which are expressed as fibers >5 μm in length/cc, a conversion factor is needed. Attempts to formulate such a conversion have generally been unsuccessful because of exceptionally large variability. This is to be expected as ambient levels are generally determined using electron microscopy whereas phase contrast microscopy is used to measure occupational exposures. In addition, techniques used to prepare samples for electron microscope observation may cause alterations in fiber size (diameter and length) distributions.

Lynch and Ayer (1966) presented results of environmental studies in the asbestos textile industry where fiber concentrations were determined using phase contrast optical microscopy and fiber size distributions were determined using electron microscopy. The mass of chrysotile on the filter was estimated by using atomic absorption spectroscopy to determine the magnesium content of the sample and asbestos content was calculated, assuming a 25% magnesium content for chrysotile. These data are summarized in Table IV-4. Based on the magnesium analysis, the authors concluded that

one nanogram of asbestos was roughly equivalent to five fibers greater than 5 μm in length by optical microscopy, although much variability about this value was observed. By using fiber size data determined by electron microscopy to calculate the mass of a typical fiber, the authors concluded that one nanogram of asbestos corresponded to 8 fibers (all lengths) by optical microscopy.

In a subsequent paper, Lynch et al (1970) published results of count to weight comparisons for other industrial operations using the sample techniques previously described. These data are summarized in Table IV-5. Again, large variations in the relationships were observed, as evidenced by large geometric standard deviations. Table IV-5 shows that one nanogram of asbestos may be roughly equivalent to 6.7 - 46.5 fibers >5 μm, depending on the operation.

In their study of asbestos contamination in commercial building, Nicholson et al (1975a) compared the results of asbestos concentrations (ng/m^3) determined by electron microscopy to fiber concentrations determined by phase contrast microscopy for the same samples. These data were highly variant showing no consistent relationship. One nanogram of asbestos was shown to range from none detected to 6,570 asbestos fibers >5 μm by phase contrast microscopy. By averaging data, it was calculated that one nanogram was equivalent to 52 asbestos fibers >5 μm in length.

Air samples collected in communities surrounding the Reserve Mining Company, Silver Bay, Minnesota, have been analyzed by electron microscopy and concentrations expressed in ng/m^3 by mass calculation and $fibers/m^3$ by direct counts (Nicholson, 1973). These results showed one nanogram of

amphibole fibers to be equivalent to 640-108,000 total amphibole fibers by electron microscopy, with an average value of 30,600 fibers/ng.

A study recently published by Dement et al (1975) provides additional data for the conversion of mass concentration to fiber number for amphiboles. In this study, 22 air samples collected in an underground gold mine were analyzed by phase contrast optical microscopy and electron microscopy to determine fiber concentrations. A direct clearing technique which preserved the original fiber size distribution was used to prepare samples for electron microscopy. In addition to fiber counts by electron microscopy, each fiber was sized (length and diameter) so that the mass could be calculated (assuming a density of 2.5 g/cc). These data are summarized in Table IV-6. From these data, approximate relationships between mass concentrations and fiber count concentrations were calculated. One nanogram was calculated to be equivalent to approximately 1,200 total fibers by electron microscopy or 400 fibers >5 μm in length by phase contrast microscopy.

The above studies have not shown a consistent conversion factor for fiber mass to fiber count. Bruchman and Rubino (1975) have suggested a conversion ratio of 20 asbestos fibers >5 μm in length, as determined by optical microscopy, per nanogram of asbestos. Based on the above review, the validity of such a general conversion may be seriously questioned.

Nonoccupational Exposures - Ambient Levels

Asbestos air pollution in urban areas has been studied. Levels of chrysotile asbestos at various locations in New York City, Philadelphia,

Ridgewood, NJ, and Port Allegany, Pa, have been studied by electron microscopy (Selikoff et al, 1972). Sample sites were chosen which were distant from any known significant source of asbestos. Study results summarized in Table IV-7 show concentrations ranging from 11 to 100 nanograms/cubic meter of air (ng/m^3). These authors point out that one nanogram of asbestos could represent a million chrysotile fibrils.

Ambient samples have been collected in the cities of Reading and Rochdale, England, Bochum and Dusseldorf, Germany, Prague and Pilsen, Czechoslovakia, Johannesburg, South Africa, and Reykjavik, Iceland (Holt and Young, 1973). Although no effort was made to quantitate levels, electron microscopy studies revealed the presence of chrysotile asbestos in most samples.

Results of electron microscopy studies of ambient samples in the United Kingdom are summarized in Table IV-8. Chrysotile concentrations of 1/10 ng/m3 were observed (Richards, 1973).

Asbestos levels in major US cities during 1969-1970 have been determined under contract with the US Environmental Protection Agency (Nicholson, 1971).Samples were collected on three or four different occasions for each city and analyzed by electron microscopy. Results are summarized in Table IV-9 and show that mean concentrations for the samples range from 0.7 to 24.3 ng/m^3;however, 48% of the cities had average concentrations less than 2.0 ng/m^3. The highest mean, 24.3 ng/m^3, was observed in Dayton, Ohio, where numerous plants processing asbestos are located. The highest concentration of 95 ng/m^3 was also observed in Dayton.

Results of chrysotile measurements within buildings insulated with asbestos and ambient levels in the vicinity of these buildings have been presented (Nicholson et al, 1975). Crysotile concentrations were determined using electron microscopy techniques as in previous studies (Selikoff et al, 1972). Ambient levels were found to range from 0 to 46 ng/m^3. Using phase contrast optical microscopy, fiber levels (ambient and indoor) were found to range from 0.000 to 0.027 fibers >5 μm/cc, with an average of 0.006 fibers/cc. Average concentrations within the building sampled ranged from 2.5 to 200 ng/m^3, indicating the possibility of fiber erosion from insulated air plenums. The same report indicates that asbestos concentrations in excess of 100 ng/m^3 may often be found in the homes of asbestos workers, with the highest measured concentration being 5,000 ng/m^3. These authors suggest that exposure in excess of 100 ng/m^3 may be associated with an observable risk of asbestos disease.

Nicholson et al (1975a) published data indicating that 35 rooms in 17 office buildings in Boston, New York, Chicago, and San Francisco-Berkeley had a mean concentration of asbestos fibers in their airs of $11,600/m^3$ whereas the intake airs for 15 of these buildings (all for which such data was given) contained a mean of 6,000 fibers/m^3. One room had a concentration of 102,800 fibers/m^3, all the others having fiber counts below $60,000/m^3$. Samples of air from plenums in 11 of these buildings contained a mean concentration of 5,100 fibers/m^3. In an earlier report (1975b), the same investigators stated that two buildings in New York in which no asbestos was known to have been used as a fireproofing or anechoic material had a mean concentration of asbestos within their circulating airs considerably above that of the intake airs for these buildings. These

findings indicate that, although pick-up of asbestos from linings applied to air-ducts and plenums may be a factor in the distribution of these fibers within buildings, these linings are not a major source of the asbestos fibers found in the air circulating within buildings.

A survey carried out in the United Kingdom (Wagg, quoted by Meyer, 1976) has shown that 82% of 73 buildings examined had airborne concentrations of asbestos fibers of up to 20,000/m^3. Only 4% had concentrations of asbestos in the range 50,000-80,000 fibers/m^3. No higher concentrations were reported. The higher concentrations were found in office buildings, residences, and miscellaneous types of buildings. Really high concentrations of asbestos in air (of the order of 1-100 ng/m^3) have been found only within a few hundred meters downwind of asbestos processing plants (Richards and Badami, 1971, 1973;Simecek, 1967; Meyer, 1976).

Asbestos fiber levels in communities surrounding the Reserve Mining Company's milling operations in Silver Bay, Minnesota, have been reported by numerous investigators. Recent preliminary air sampling results have been reported for ten stations located between the Reserve Mining Company pollution source and several population centers (Fairless, 1974). Samples were collected each 6th day, beginning on November 6, 1974, (for a 1-year period). These samples were submitted blind to one or more of three laboratories where asbestos fibers concentrations were determined by electron microscopy. Results of these preliminary analyses are summarized in Table IV-10. Mean concentrations of amphibole fibers ranged from 2.6 to 8.9 x 10^3 fibers/m^3. In addition to amphibole fibers, chrysotile concentrations for individual samples ranged from none detected to 10.4 x 10^4 fibers/m^3. Analyses of all samples collected have not been completed.

[illegible] amphibole fibers. chrysotile

Concentrations of amphibole fibers have also been reported near specific point emission sources of the Reserve Mining Company (Nicholson et al, 1974). Concentrations as high as 11 x 10^6 fibers/m^3 of air were reported.

NIOSH has performed two studies of fiber concentrations in the air of public buildings using the phase contrast microscopy counting technique (Wallingford et al, 1973; Zumwalde, 1973). Samples were collected over 6-8 hours at 7 - 10.5 liters/minute. These data are summarized in Table IV-11. Mean concentrations of 0.004 and 0.001 fibers >5 μm were observed, with the highest single concentration observed being 0.008 fiber >5 μm/cc.

In summary, ambient asbestos levels as determined by electron microscopy techniques are generally less than 10 ng/m^3 with occasional peaks as high as 100 ng/m^3. Only a few studies of ambient levels have been performed using phase contrast optical microscopy. These studies indicate ambient levels to be generally less than 0.01 fibers >5 μm/cc, with some peak values as high as 0.03 fibers >5 μm/cc.

REFERENCES FOR CHAPTER IV

1. Langer AM, Mackler AD, Pooley FD (1974): Electron microscopical investigations of asbestos fibers. Environ Health Pers 9:63-80

2. Timbrell V (1970): Characteristics of the VICC standard reference samples of asbestos, in Shapiro H (ed): Proceedings International Conference on Pneumoconiosis, Johannesburg. New York, Oxford University Press

3. Cook PM, Rubin JB, Maggiore CJ, Nicholson WJ (1974): X-ray diffraction and electron beam analysis of asbestiform minerals in Lake Superior waters

4. Rubin JB, Maggiore CJ (1974): Elemental analysis of asbestos fibers by means of electron probe techniques. Environ Health Pers 9:81-84

5. Ferrell RE, Paulson GG, Walker CW (1974): Evaluation of any SEM-EDS method for identification of chrysotile. Scanning Electron Microsc Part II: 537-46

6. Maggiore CJ, Rubin IB (1973): Optimization for a SEM x-ray spectormeter system for the identification and characterization of ultramicroscope particles. Scanning Electron Microsc Part I: 129-36

7. Langer AM, Rubin I, Selikoff IJ (1975): Electron microprobe analysis of asbestos bodies. Histochem Cytochem J 20:735-40

8. Dement JM, Zumwalde RD, Wallingford KM (19 75): Asbestos fiber exposures in a hard rock gold mine. Ann N Y Acad Sci 271:345-52

9. Nicholson WJ (1974): Analysis of amphibole asbestiform fibers in municipal water supplies. Environ Health Pers 9:165-72

10. Porter MC, Berggren RG (1974): Removal and detection of liquid borned asbestos fibers with nuclepore membrance. Pleasanton, Calif, Nuclepore Corporation, Dec. 24, 1974

11. Beaman DR, File DM (1975) The quantitative determination of asbestos fiber concentrations. The Dow Chemical Company (unpublished report)

12. Ortiz LW, Loom BL (1974): Transfer technique for electron microscopy of membrane filter samples. Am Ind Hyg Assoc J: 423-25

13. Selikoff IJ, Nicholson WJ, Langer AM (1972): Asbestos air pollution. Arch Environ Health 25:1-13

14. Stanley HD, Norwood RE (1974): The detection and identification of asbestos and asbestiform minerals in talc, in Proceedings of the Burea of Mines Talc Symposium, Washington, D C

15. Rohl AN, Langer AM (1974): Identification and quantitation of asbestos in talc. Environ Health Pers 9:95-109

16. Crable JV, Knott MJ (1968): Application of x-ray diffraction analysis of crocidolite and amosite in bulk or settled dust samples. Am Ind Hyg J 27:383-85

17. Crable JV, Knott MJ (1966): Quantitative determination of chrysotile amosite and crocidolite by x-ray diffraction. Am Ind Hyg J 27: 449-53

18. Keenan RG, Lynch JR (1970): Techniques for the detection, identification and analysis of fibers. Am Ind Hyg J 31:587-97

19. Birks LS, Fatemi M, Gilfrich JV, Johnson ET (1975): Quantitative analysis of airborned asbestos by x-ray diffraction: Feasibility study AD-A007530, Naval Res Lab, Washington, DC

20. Schlez JP (1974): The detection of chrysotile asbestos at low levels in talc by differential thermal analysis. Thermochemica Acta 8:197-203

21. Julian Y, McCrone WC (1970): Identification of asbestos fibers by microscopical dispersion staining. Microscope 18:1-10

22. McCrone WC, Stewart IM (1974): Asbestos. American Laboratory, April

23. US Dept of Labor, Occupational Safety and Health Administration (1975): Occupational Safety and Health Standards. Fed Reg 29 CFR 1910.1001, 1975

24. Corn M, Sansone EC (1974): Determination of total suspended particulate matter and airborne fiber concentrations at three fibrous glass manufacturing facilities. Environ Res 8:37-52

25. Leidel NA, Busch KA (1974): An evlauation of phase contrast microscopes for asbestos counting. Presented at the 1974 American Industrial Hygiene Conference, Miami Beach, Florida, May 18, 1974

26. Conway RE, Holland WD (1973): Statistical evaluation of the procedures for counting asbestos fibers on membrane filters. LFE Corp., Richmond, CA. Prepared for Asbestos Information Association/North America, New York, 1973

27. Rajhans GS, Bragg GM (1975): A statistical analysis of asbestos fiber counting in the laboratory and industrial environment. Am Ind Hyg Assoc J 36:909-15

28. Leidel AL, Bayer SG, Zumwalde RD (1975): SUPHS/NIOSH Membrane Filter Method for Evaluating Airborne Asbestos Fibers. US Dept Health, Education, and Welfare, Public Health Service, Center for Disease Control, National Institute for Occupational Safety and Health, November 1975 (in print)

29. Lynch JL, Ayer HE (1966): Measurement of asbestos dust exposure in the asbestos textile industry. Am Ind Hyg Assoc J 27:43-37

30. Lynch JL, Ayer HE, Johnson DL (1970): The interrelationships of selected asbestos exposed indices. Am Ind Hyg Assoc J 31:598-604

31. Nicholson WJ, Rohl AN, Weisman I (1975a): Asbestos Contamination of the air in public buildings. Final report to the Environmental Protection Agency, Contract No. 68-02-1346

32. Nicholson, WJ (1973): Testimony, United States versus Reserve Mining Company, No. 5-72-Civil-19, Sept. 6, 1973. Exhibit No. 62.

33. Bruckman L, and Burino R (1975): Asbestos--Rationale behind a proposed air quality standard. J Air Pollut Control Assoc 25: 12

34. Holt PF, Young DK (1973): Asbestos fibers in the air of towns. Atmos Environ 7:481-83

35. Richards AL (1973): Estimation of submicrogram quantities of chrysotile asbestos by electron microscopy. Anal Chem 45: 809-11

36. Nicholson WJ (1971): Measurement of asbestos in ambient air. Final report to the Environmental Protection Agency, Contract EPA 70-92

37. Fairless B (1974): Asbestos fiber concentrations in air samples taken from areas near the western arm of Lak Superior, Progress Report, US Environmental Protection Agency Region V, Chicago, Illinois.

38. Nicholson W (1973): U.S. District Court for Minnesota. United States versus Reserve Mining Company. No. 5-72-Civil-19, Sept. 6, Exhibit No. 62

39. Wallingford KM, Bierbaum PJ, Dement JM (1973): Determination of asbestos levels in a public building located in Towson, Maryland, EIB, DFSCI, NIOSH

40. Zumwalde, R.D. (1973): Asbestos survey of Federal Office Building #7, U.S. Court of Claims and Court of Customs and Patent Appeals Building, Washington, D.C. and George H. Fallon, Office Building, Baltimore, Maryland EIB, DFSCI, NIOSH

41. Nicholson WJ, Rohl AN, Weisman I (1975b): Asbestos Contamination of Building Air Supply Systems. Paper given at Las Vegas, Nevada, 14-19 September, 1975

42. Meyer PD (1976): Sampling and Detection of Asbestos in Air, Food, Soil and Water. Paper prepared by RVO TNO for European Economic Community, 1976

43. Richards AL, Badami DV (1971): Chrysotile Asbestos in Urban Air. Nature 243:93-94

44. Simecek J (1967): Measuring Asbestos Dust. Staub - Reinhalt Luft 27:20-23

TABLE IV-1

TYPICAL OPTICAL DATA FOR ASBESTOS MINERALS

Asbestos Type	Crystal System	Refractive Indices	Extinction Angles	Sign of Elongation
Chrysotile	monoclinic	1.49-1.57	yAL* = 0^{o}	+
Anthophyllite	orthorhombic	1.60-1.66	yAL = 0^{o}	+
Amosite	monoclinic	1.66-1.70	yAL = $14\text{-}21^{o}$	+
Crocidolite	"	1.69-1.71	yAL = $3\text{-}15^{o}$	-
Tremolite**	"	1.60-1.65	yAL = $10\text{-}21^{o}$	+
Actinolite **	"	1.62-1.68	yAL = $10\text{-}15^{o}$	+

*L = long direction of fibers
** Tremolite and actinolite form a continuous mineralogical series.
Values shown are for end members.

TABLE IV-2

DISPERSION STAINING COLORS FOR ASBESTOS MINERALS
USING PLANE POLARIZED LIGHT

Asbestos Type	Refractive Index Liquid	Dispersion Staining Colors	
Chrysotile	1.560	light blue	magenta
Anthophyllite	1.610	blue-green	golden yellow
Amosite	1.670	red magenta	"
Crocidolite	1.700	magenta	blue magenta

TABLE IV-3

THEORETICAL MINIMUM DETECTABLE FIBER CONCENTRATIONS BY PHASE CONTRAST OPTICAL MICROSCOPY

Sampling Period (Minutes)	Minimum Detectable Conc. fibers >5 μm/cc
15	0.04
30	0.02
60	0.01
90	0.007
120	0.005
240	0.003
480	0.001

*Based on a sample flow rate of 2.01 lpm and a microscope counting field area of 0.0071 mm^2.

TABLE IV-4

ASBESTOS COUNT/WEIGHT RELATIONSHIPS FOR ASBESTOS TEXTILE PLANTS

Type Count By Phase Contrast Microscopy	Fibers per Nanogram of Asbestos
Total Fibers	11
>5 μm Fibers	5

From Lynch and Ayer (1966)

TABLE IV-5

ASBESTOS COUNT/WEIGHT RELATIONSHIPS FOR VARIOUS INDUSTRIAL OPERATIONS

Product	Type Fiber Count	Geometric Mean Fibers/ng	Geometric Standard Deviation
Textile	Total	14.5	2.5
	>5 μm	6.7	3.3
Friction	Total	26.3	3.4
	>5 μm	13.9	3.6
Pipe	Total	46.5	2.8
	>5 μm	22.5	2.9

From Lynch and Ayer (1966)

TABLE IV-6

SUMMARY OF FIBER COUNT/MASS RELATIONSHIPS

Analysis Method	Average Conc. (range)	Units of Measure
Total Fibers by Electron Microscopy	4.82 (0.66 - 11.79)	fibers/cc
Asbestos Mass by Electron Microscopy	3,900 (540 - 9600)	ng/m^3
Fibers >5 μm by Optical Microscopy	1.51 (0.16 - 2.8)	fibers/cc

Approximate Relationships:
1 ng $\cong$ 1,200 total fibers by electron microscopy
1 mg $\cong$ 400 fibers >5 μm in length by phase contrast microscopy
From Dement et al (1975)

TABLE IV-7

SUMMARY OF AMBIENT ASBESTOS LEVELS IN VARIOUS CITIES

Sample Site	Asbestos Conc. 10^{-9} gm/m^3
New York City	25-60
Manhattan	25-28
Bronx	19-22
Queens	18-29
Staten Island	11-21
Philadelphia, Pa.	45-100
Ridgewood, N.J.	20
Port Allegany, Pa.	10-30

From Selikoff et al (1972)

TABLE IV-8

SUMMARY OF AMBIENT CHRYSOTILE LEVELS
IN THE UNITED KINGDOM

Sample Site	Chrysotile Conc. 10^{-9} gm/m^3
Rochdale (Factory Grounds)	1-10
Rochdale (Town Center)	10
Lancashire/Yorkshire	1-10
Industrial Site (Oldbury)	10

From Richards (1973)

TABLE IV-9

SUMMARY OF AMBIENT ASBESTOS LEVELS
IN 49 CITIES FOR 1969-1970

Conc. 10^{-9} gm/m^3	Cumulative % of City Mean Conc. $\leq$ Given Conc.
0.1-1.9	12
1.0-1.9	48
2.0-2.9	64
3.0-3.9	72
94.0-4.9	86
5.0-5.9	94
>6.0*	6%

*Highest Mean - 24.3 ng/m^3 observed in Dayton, Ohio
From Nicholson et al (1971)

TABLE IV-10

SUMMARY OF AMPHIBOLE FIBER CONCENTRATIONS
FOR TEN SAMPLE SITES IN THE VICINITY OF RESERVE MINING

Sample Site	Amphibole Conc. 10^{-9}fibers/m^3	
	Mean	Range
Duluth	7.5	0-17
Duluth (Residence)	2.6	0- 8
Silver Day (Residence)	11	0-30
Babbit (Residence)	13	0-82
Hoyt Lake	8.5	0-31
Hibbing	5.6	0.19
Cloquet	6.8	0-30
Pengilly	6.6	0-17
Virginia	4.2	0-12
Mt. Iron	8.9	0-45

Overall Mean = 7.6 X 10^{-9}fibers/m^3
From Fairless (1974)

TABLE IV-11

SUMMARY OF FIBER CONCENTRATION DETERMINATIONS IN THE AIR OF PUBLIC BUILDINGS USING PHASE CONTRAST OPTICAL MICROSCOPY

Building Location	Fibers >5 μm in Length/cc Mean and Range
Baltimore, Maryland and Washington, D.C.	0.004 (0.001-0.008)
Towson, Maryland	0.001 (0.000-0.003)

From Wallingford et al (1973) and Zumwalde (1973)

V. BASIS FOR THE RECOMMENDED STANDARD

The first modern approach to the setting of an asbestos standard was proposed by the British Occupational Hygiene Society (BOHS 1968) in terms of fiber concentration. In 1968, a subcommittee of the Society evaluated data on 290 men at work in an asbestos factory. These data were provided by company sources. All the men had been employed after January 1933, following implementation of dust control measures mandated by the Factory Inspectorate in 1931. Estimates of the fiber exposure of these workmen were also provided by the company. Of the 290 individuals, 8 were stated to have x-ray evidence of asbestos disease and 16 had rales. Noteworthy in the 1968 data was the preponderance of individuals who had been employed less than 20 years. Only 118 of the 290 persons had worked for longer than 20 years and a scant 13 has been employed for 30 or more years.

After a review of these data, the BOHS proposed a standard which was adopted with minor modifications by the British government in 1969, and implemented in May 1970. All fibers between 5 and 100 microns in length were counted by light microscopy. The standard required no action to be taken below .2 fibers/cc. Between 2 fibers/cc and 12 fibers/cc, control measures commensurate with the exposure circumstances (time and frequency of worker exposure) were prescribed; above 12 fibers/cc, full application of control measures, including respiratory protection, was mandatory. The BOHS predicted that the risk of being affected, to the extent of having the earliest clinical signs of asbestos exposure (rales), would be less than 1% for an accumulated exposure of 100 fiber-years/cc (2 fibers/cc for 50

years, 4 fibers/cc for 25, etc). Data (Lewinsohn, 1972) from the same factory which formed the basis for the BOHS standard demonstrate that a greater prevalence of abnormalities now exist (Table V-1). These data, in addition to demonstrating a dose-response relationship for radiographically detected abnormalities consistent with asbestosis, further showed a 17% prevalence of abnormal radiographic findings (6% consistent with asbestosis) in individuals employed since 1950.

Weill et al (1975), when considering lung function and irregular small opacities, reported that there was little evidence of a dose-response relationship below 100 mppcf-years. They further concluded that a concentration of 5 fibers/cc could be cautiously considered as "safe". Ayer and Berg (1976), however, reported data which suggest that the BOHS standard, of an average cumulative exposure of 100 fiber-years/cc, for chrysotile asbestos may prevent significant decreases in pulmonary function only when combined with periodic spirometry and further reduction of exposure for affected workers. Holmes (1973) has since stated that the data upon which the BOHS standard was based were inadequate to set a standard to prevent asbestosis. The BOHS-recommended standard of 2 fibers/cc was based on data related only to asbestosis and the Society clearly cautioned that, since a quantitative relationship between asbestos exposure and cancer risk was not known, it was not possible at that time to specify an air concentration which was known to be free of increased cancer risk. (BOHS 1968)

Howard et al (1976), in a follow-up examination of the textile workers previously studied by Doll (1955) and Knox et al (1965, 1968) for cancer, and by Lewinsohn (1972) for asbestosis, reported a statistically

significant increase in the risk of developing lung cancer (1.8 times the expected) among those first entering scheduled areas from 1933 to 1950. In the same study, they also reported an excess of deaths due to lung cancer (1.9 times the expected) after 15 or more years from initial exposure among those who started work subsequent to 1950, a period of improved industrial engineering control technology and regulation.

In a study of miners exposed to amphibole fibers (amosite) in the cummingtonite-grunerite ore series, with airborne concentrations of less than 2.0 fibers/cc (average concentration, 0.25 fibers/cc) and 94% of the fibers shorter than 5 μm in length, Gillam et al (1976) have demonstrated threefold increases in the risks of mortality from both malignant and nonmalignant respiratory diseases.

Newhouse (1969, 1973) and Newhouse et al (1972) have shown that the cancer risk to factory workers following mixed exposure to chrysotile, amosite, and crocidolite is dose-related. The women reported to have heavier exposures (as judged by their occupations) showed a sixfold excess of cancer following only 15 years' latency, whereas those with moderate or low exposures required 25 years' latency to demonstrate an excess. The rate of mesothelioma increased with both the severity and the length of exposure. However, even with as little as two years of asbestos exposure, six mesotheliomas occurred among female employees.

McDonald (1973) stated that the risk of developing lung cancer was essentially confined to persons with a dust index above 200 mppcf-years, and Enterline et al (1973) showed no direct dose-response for respiratory cancer below 125 mppcf-years. In a review of these two papers, Schneiderman (1974) concluded that, instead of being consistent with a

threshold level at which no cancer risk exists, these data did not provide evidence for a threshold or for a "safe" level of exposure. He pointed out that in the paper by Enterline et al (1973) there is no dose group for which the Standardized Mortality Ratio (SMR) is below 100 (100 = normal), but that the 95% confidence limits on the SMR's included 100 for two of the three dose groups below 125 mppcf-years. One of the dose groups (25-62.4) had a statistically significant excess mortality from lung cancer, whereas for the other two this mortality rate was insignificantly elevated above the expected values. Regarding McDonald's paper, Schneiderman stated that it is hard to determine what is excess since no expected numbers for each group were given upon which to base this comparison.

Among amosite workers with employment of 3 months or less, Selikoff (1976) reported excess cancer risks of 3.87, 1.68, and 1.65 times those expected for cancer of the lung, colon and rectum, and all sites, respectively.

Anderson et al (1976) have reported a significant excess of radiographic abnormalities of the chest characteristic of asbestos exposure (pleural and/or parenchymal) 25 - 30 years after the onset of household contamination. These abnormalities were observed in 35% of 326 otherwise healthy workers who had household contacts with amosite asbestos. In addition, four pleural mesotheliomas were found in this group.

VI. THE RECOMMENDED STANDARD

Available studies provide conclusive evidence that exposure to asbestos fibers causes cancer and asbestosis in man. Lung cancers and asbestosis have occurred following exposure to chrysotile, crocidolite, amosite, and anthophyllite. Mesotheliomas, lung and gastrointestinal cancers have been shown to be excessive in occupationally exposed persons, while mesotheliomas have developed also in individuals living in the neighborhood of asbestos factories and near crocidolite deposits, and in persons living with asbestos workers. Asbestosis has been identified among persons living near anthophyllite deposits.

Likewise, all commercial forms of asbestos are carcinogenic in rats, producing lung carcinomas and mesotheliomas following their inhalation, and mesotheliomas after intrapleural or ip injection. Mesotheliomas and lung cancers were induced following even 1 day's exposure by inhalation.

The size and shape of the fibers are important factors; fibers less than 0.5 μm in diameter are most active in producing tumors. Other fibers of a similar size, including glass fibers, can also produce mesotheliomas following intrapleural or ip injection.

There are data that show that the lower the exposure, the lower the risk of developing cancer. Excessive cancer risks have been demonstrated at all fiber concentrations studied to date. Evaluation of all available human data provides no evidence for a threshold or for a "safe" level of asbestos exposure.

In view of the above, the standard should be set at the lowest level detectable by available analytical techniques, an approach consistent with NIOSH's most recent recommendations for other carcinogens (ie, arsenic and vinyl chloride). Such a standard should also prevent the development of asbestosis.

Since phase contrast microscopy is the only generally available and practical analytical technique at the present time, this level is defined as 100,000 fibers >5 μm in length/m^3 (0.1 fibers/cc), on an 8-hour-TWA basis with peak concentrations not exceeding 500,000 fibers >5 μm in length/m^3 (0.5 fibers/cc) based on a 15-minute sample period. Sampling and analytical techniques should be performed as specified by NIOSH publication USPHS/NIOSH Membrane Filter Method for Evaluating Airborne Asbestos Fibers - T.R. 84 (1976).

This recommended standard of 100,000 fibers >5 μm in length/m^3 is intended to (1) protect against the noncarcinogenic effects of asbestos, (2) materially reduce the risk of asbestos-induced cancer (only a ban can assure protection against carcinogenic effects of asbestos) and (3) be measured by techniques that are valid, reproducible, and available to industry and official agencies.

However, some difficulties arise in that specific work practices and innovative engineering control or process changes are needed. But because of the well-documented human carcinogenicity from all forms of asbestos, these difficulties should not be cited as cause for permitting continued exposure to asbestos at concentrations above 100,000 fibers >5 μm in length/m^3.

This standard was not designed for the population-at-large, and any extrapolation beyond general occupational exposures is not warranted. The standard was designed only for the processing, manufacturing, and use of asbestos and asbestos-containing products as applicable under the Occupational Safety and Health Act of 1970.

REFERENCES FOR CHAPTERS V AND VI

1. 1969 Standard for asbestos dust concentration for use with the asbestos regulations. Department of Employment and Productivity, Her Majesty's Factory Inspectorate. Technical Note 13, 1970

2. Lewinsohn HC (1972): The medical surveillance of asbestos workers. Soc Health 92:69

3. Weill H, Ziskind MM, Waggenspack C, Possiter CE (1975): Lung function consequences of dust exposure in asbestos cement manufacturing plants. Arch Environ Health 30:248-52

4. Ayer H, Berg J (1976): Cumulative asbestos exposure and forced vital capacity. Submitted for publication to Arch Environ Health

5. Holmes S (1973): Environmental data in industry, in Bogovski P, Timbrell V. Gilson JC, Wagner JC (eds): Proceedings of the Conference on Biological Effects of Asbestos. Lyon, pp 135

6. Newhouse ML (1969): A study of the mortality of workers in an asbestos factory. Br J Ind Med 26:294

7. Newhouse ML (1973): Cancer among workers in the asbestos textile industry, in Bogovski P, Gilson JC, Timbrell V, Wagner JC (eds): Proceedings of the Conference on Biological Effects of Asbestos. Lyon, pp 203

8. Newhouse ML, Berry G, Wagner JC, Turok ME (1972): A study of the mortality of female asbestos workers. Br J Ind Med 29:134

9. Howard S, Kimben LJ, Lewinsohn HC, Peto J, Doll R (1976); A Mortality Study among Workers in an Englosh Asbestos Factory. Oxford University, (in press)

10. Doll R (1955): Mortality from lung cancer in asbestos workers. Br J Ind Med 12:81-86

11. Knox JF, Doll RS, Hill ID (1965): Cohort analysis of changes in incidence of bronchial carcinoma in a textile asbestos factory. Am NY Acad Sci 132:526-35

12. Knox JF, Holms S, Doll R, Hill ID (1968): Mortality from lung cancer and other causes among workers in an asbestos textile factory. Br J Ind Med 25:293-303

13. Gillam JD, Dement JM, Lemen RA, Wagoner JK, Archer VE, Beljer HP (1976): Mortality patterns among hard rock gold miners exposed to an asbestiform mineral. Ann NY Acad Sci 271:336-44

TABLE VI-1

B.O.H.S. ASBESTOS STANDARD
X-RAY FINDINGS IN AN ASBESTOS TEXTILE FACTORY
DECEMBER 1970 (MALES)

Years of Exposure	No.	X-ray Findings			
		Normal	Pleural Fibrosis*	Pulmonary Fibrosis	Total Abnormal**
0 - 9	613	548	10	0	65(11%)
10 - 19	189	122	18	20	67(36%)
20 - 29	114	51	30	21	63(55%)
30 - 39	42	9	17	17	33(78%)
40 - 49	12	2	6	3	10(83%)

* Consistent with asbestos exposure
**Including changes not considered due to asbestos exposure
Adapted from reference 2

☆U.S. GOVERNMENT PRINTING OFFICE: 1986-646-117/40905

DEPARTMENT OF
HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
CENTER FOR DISEASE CONTROL
NATIONAL INSTITUTE FOR OCCUPATIONAL SAFETY AND HEALTH
ROBERT A. TAFT LABORATORIES
4676 COLUMBIA PARKWAY, CINCINNATI, OHIO 45226

OFFICIAL BUSINESS
PENALTY FOR PRIVATE USE, $300

POSTAGE AND FEES PAID
U.S. DEPARTMENT OF H.E.W
HEW 396

THIRD-CLASS MAIL

DHEW (NIOSH) Publication No. 77-169