1. INTRODUCTION

Adverse health effects from exposure to grain dust were first reported in 1713, when Bernardino Ramazzini noted that grain dust irritated the throats, eyes, skin, and lungs of grain workers (Ramazzini 1713). Workers may be exposed to grain dust during farming operations or while working at grain elevators and flour, feed, and seed mills. Exposure to grain dust may also occur during the transportation of grain between these facilities. Present-day grain workers have been reported to exhibit both pulmonary effects (including cough, dyspnea, wheezing, asthma, chronic bronchitis, farmer's lung, chronic airway obstruction, mycotoxicosis, and allergic alveolitis) and nonpulmonary effects (including conjunctivitis, rhinitis, grain fever, and dermatitis).

In the United States of America (U.S.A.), the National Institute for Occupational Safety and Health (NIOSH) has previously considered the explosive properties of grain dust and has recommended safe work practices and engineering controls (NIOSH 1983a). In Sweden, Lantbrukets Brandskyddskommitte has issued recommendations on how to prevent the spontaneous combustion and explosion of grain dust (SBK 1977). Data have also been reported on grain dust contaminants, which include fungal spores, bacteria, mites, and insect body parts (NIOSH 1986a).

This paper addresses the adverse health effects of human exposure to grain dust. A thorough search of the literature has identified three groups of studies specifically dealing with this type of occupational exposure. These epidemiologic studies are discussed in detail in Section 5.7.

2. CHARACTERISTICS AND COMPOSITION OF GRAIN DUST

Grain dust consists of 60% to 75% organic material and 25% to 40% inorganic material (Yoshida and Maybank 1980), including the following:

(1) Fragments of cereal grains (e.g., wheat, oats, barley, rye, and corn), oil seeds (e.g., rapeseed, linseed, and sunflower seed), and pulses (the edible seeds of legumes such as peas and soybeans) (Becklake 1980),

(2) Decomposition products of grains, seeds, and pulses (Chan-Yeung and

Ashley 1978),

(3) Inorganic materials such as soil and traces of chemical elements (Yoshida and Maybank 1980),

(4) Microorganisms (NIOSH 1986a, 1986b),

(5) Insects, insect parts, and mites (Labour Canada 1981),

(6) Hairs, feathers, and excreta of rodents and birds (Becklake 1980),

(7) Fragments of plant matter (Becklake 1980),

(8) Chemicals such as fertilizers, pesticides, and herbicides (Federal Register 1980), and

(9) Other contaminants such as metal fragments, lubricating oils, or paint chips that may have accumulated with the grain during the harvesting and subsequent processing or storage (Labour Canada 1981).

Airborne grain dust concentrations in storage and grain-handling facilities are affected by the design of ventilation systems (if present), the intensity and thoroughness of housekeeping efforts, the amounts of contaminants present, the humidity, the age of the grain, the extent to which the grain has been cleaned, and the degree to which the grain has been manipulated.

2.1 Microorganisms

The microbial flora associated with grain dust consist of a wide variety of fungi and bacteria. The predominant organisms isolated from grain dust depend on the time the dust is produced (during harvest or storage) and factors such as original growing conditions, season of the year, geographical location, water content of the grain, temperature, type of grain, and storage practices. Some organisms invade or contaminate the grain when it is developing in the fields, and other organisms are primarily associated with grain during storage (Lacey 1980; NIOSH 1986a).

Under field conditions, fungi such as Cladosporium, Alternaria, Fusarium, Diplodia, Chaetomium, Rhizopus, and Absidia are predominant, but bacteria such as Erwinia herbicola, Pseudomonas, Bacillus, and Streptomyces are also found (NIOSH 1986a). Though microorganisms from the field can still be isolated after the grain has been stored, the number of field organisms usually declines over time, and some are replaced by other fungi and bacteria (Lacey 1980). Aspergillus and Penicillium species are the predominant fungi associated with storage, but grain that has become moist or heated often contains Micropolyspora, Thermoactinomyces vulgaris, and yeasts such as Candida, Mucor pusillus, and Absidia (NIOSH 1986a). Appendix Table A-1 lists the predominant microorganisms identified in selected reports.

2.2 Pesticides

Grain may be fumigated with pesticides at a number of points between the field and storage facility to prevent spoilage or loss from pests. Fumigation frequently occurs during transportation by truck or freight car to large elevators. Grain may be fumigated again during transfer into elevators, during storage, and also during discharge into barges, ships, or rail cars. Grain in long-term storage is subjected to periodic preventive fumigation and treatment if pest infestation occurs.

Pesticides that are currently banned for use with grain in the U.S.A. are ethylene dibromide (Federal Register 1984), carbon disulfide, ethylene dichloride, and carbon tetrachloride (Federal Register 1985). Pesticides that are currently being used are methyl bromide (EPA 1986), and aluminum or magnesium phosphide (EPA 1987). Malathion has an EPA label registration that permits it to be used for protecting grain from future infestation. Sampling has been conducted for carbon disulfide, ethylene dibromide, and carbon tetrachloride (McMahon 1971; NIOSH 1977, 1984a, 1985a, 1985b); chloroform and 1,2-dichloroethylene (NIOSH 1984a, 1985a); methyl bromide and ethylene dichloride (NIOSH 1977, 1985a); carbon disulfide (NIOSH 1977, 1985b); malathion (Palmgren and Lee 1984; NIOSH 1985c); 1,2-dibromoethane (Berck 1974; Panel on Fumigant Residues in Grain 1974; Heikes 1985); phosphine (NIOSH 1977, 1985c, 1987); ethylene dichloride (Berck 1974; NIOSH 1984a); carbon tetrachloride (NIOSH 1976a); trichloroethylene, and chloroform (Panel on Fumigant Residues in Grain 1974); and diazinon

(Palmgren and Lee 1984). None of these pesticides are known to cause the major health effects identified with exposures to grain dust. NIOSH has recommended that some pesticides (e.g., carbon tetrachloride, trichloroethylene, and ethylene dibromide) be regarded as potential occupational carcinogens, and that efforts be made to substitute or take appropriate control measures (NIOSH 1976b, 1978, 1983b).

2.3 Inorganic compounds

Wirtz and Olenchock (1984a) characterized the elemental composition of airborne grain dusts from six different grains and the settled dust from grain elevators. The data from this study demonstrated that differences exist between the elemental compositions of the airborne grain dusts generated by different grains and between the compositions of settled and airborne grain dusts.

Concern exists about the silica content of grain dust. Silica has been reported to constitute 9.96% of dusts with a particle size <44 µm (Heatley et al. 1944). Stepanov et al. (1967) reported that up to 70% of the grain dust from the elevator and threshing floor of a grain elevator consisted of organic material and that the mineral fraction of the dust was composed of 8% to 18% free silica. When available, silica concentrations are reported in the epidemiologic studies in Section 5.7.

3. ANALYTICAL METHODS

Because of the variety of contaminants occurring in grain dust, the analytical methods for their determination cannot be reviewed in this brief document. The reader is referred to standard textbooks on analysis of organic chemicals in the workplace. Whether or not the specific components of the dusts are measured, the exposure measurement should involve the collection of the total and respirable fractions. These can be collected using standard methods for total nuisance dust (NIOSH Method 0500) and respirable nuisance dust (NIOSH Method 0600) (NIOSH 1984b).

Several methods are available for sampling the microflora of both settled and airborne grain dust. These methods vary in their degree of precision, sophistication, and suitability (Lacey 1980; NIOSH 1986a). Differences in collection procedures and in methods for culturing and measuring the microflora of grain dust may result in large variations in the numbers and types of microorganisms reported.

4. HUMAN EXPOSURE CONCENTRATIONS

The composition of airborne grain dust is unknown in the cited epidemiologic studies. Likewise, exposure concentrations of grain dust in the grain handling industry are largely unknown, since current and historical data are sparse. All available grain dust concentrations are given for the epidemiologic studies presented here. The low and high values for grain dust are presented by facility for Canada and the U.S.A. (Table I). Data on exposure to grain dust are listed by occupational group, process, or area monitored in Appendix Tables A-2 and A-3 for Canada and the U.S.A. In Sweden, the concentration of grain dust ranged from 4 to 53 mg/m^3 in five grain pits (ASF 1985).

5. EFFECTS IN HUMANS

This document deals with the adverse health effects of exposure to grain dust. The occurrence of these adverse health effects has been documented in the literature since 1713.

5.1 Uptake and deposition in human lungs

No information has been found regarding the uptake and deposition of grain dust in human lungs.

5.2 Acute effects

Acute exposure to grain dust has resulted in pruritic skin reactions, conjunctivitis, rhinitis, asthma, and grain fever (symptoms of the latter may include cough, chest tightness, wheezing, dyspnea [shortness of breath], expectoration, fever, chills, flushed face, and pain in the joints and muscles). See also Section 5.7, Epidemiologic studies.

5.3 Chronic effects

Chronic exposure to grain dust has resulted in chronic bronchitis and hyperreactive airways. See also Section 5.7, Epidemiologic studies. Neuropsychiatric effects have been seen in grain elevator workers exposed to carbon disulfide (Peters et al. 1982).

Table I.--Summary of area grain dust concentrations in various facilities in Canada and the U.S.A.

Location and type of facility	Number of samples	Range of means for total dust concentrations (mg/m^3)	Reference
Canada:*			
Feed mill	21	2.83 to 25.68	Schrag and Eng (1972)
Grain elevator	5	21.35	Schrag and Eng (1972)
Seed cleaning plant	7	16.26 to 19.01	Schrag and Eng (1972)
Country grain elevator	55	3.86 to 16.2	Farant and Moore (1978)
Country grain elevator	--	0.3-0.9 to 250-890	Yoshida and Maybank (1980)
Country grain elevator	--	15-105 to 80-285	Yoshida and Maybank (1980)
U.S.A.:†			
Grain elevator	--	0.2 to 70.6	NIOSH (1976a)
Grain elevator	--	2.5 to 19.9	NIOSH (1977)
Grain elevator	--	2.0 to 118.8	NIOSH (1977)
Grain elevator	--	0.2 to 6.6	NIOSH (1977)
Grain elevator	--	0.7 to 35.9	NIOSH (1977)
Grain elevator	--	0.28 to 9.5	NIOSH (1985c)
Grain elevator	--	0.34 to 30.0	NIOSH (1985c)
Grain elevator	13	0.96 to 9.48	NIOSH (1986a)

*Area dust concentrations.
†Personal dust concentrations.

5.4 Critical effects

No specific adverse health effect can be recognized as always occurring first in workers exposed to grain dust. The first effect could be manifested as irritation of the throat, eyes, skin, or lungs.

5.5 Dose response/dose effect

Table II lists the reported human health effects at various grain dust exposure concentrations.

5.6 Case studies

The following health effects have been reported in workers exposed to grain dust: silicosis in a worker who unloaded grain from rail cars (Heatley et al. 1944), pneumoconiosis in dock laborers who primarily handled grain (Dunner et al. 1946), farmer's lung in farmers who handled grain (Dickie and Rankin 1958; Patterson et al. 1974; Kotimaa et al. 1984), neuropsychiatric disorders in grain storage workers (Peters et al. 1982), pulmonary mycotoxicosis (now referred to as organic dust toxic syndrome [doPico 1986]) in farmers who handled moldy silage (Emanuel et al. 1975), and grain fever and severe dyspnea in grain elevator workers (Skoulas et al. 1964).

5.7 Epidemiologic studies

5.7.1 Studies of workers in Superior, Wisconsin, and Duluth, Minnesota, United States of America

A series of reports has been published examining the prevalence, nature, and cause of respiratory disease of grain workers in Superior, Wisconsin, and Duluth, Minnesota, U.S.A. doPico et al. (1977) reported on a November 1974 health survey of grain workers. doPico et al. (1984) reported a 1978-80 health survey of grain workers and a comparison population. The information reported in this study was subsequently published by NIOSH (1986b). A year before publication of this health survey, doPico et al. (1983) reported the results of special tests and/or analyses on subsets of those workers.

Table II.--Health effects of grain dust exposure at various concentrations

Exposure concentration (mg/m^3)*	Health effects and reference
10.3 to 253 (total)	Burning and itching eyes, nasal stuffiness, rhinorrhea, cough, expectoration, wheezing, chronic bronchitis (doPico et al. 1977)
3.3 ± 7.0 (total)	Cough, expectoration, dyspnea, eye irritation, nasal stuffiness (doPico et al. 1983)
0.9 ± 0.77 (respirable) 5.7 ± 10.9 (total)	Airway obstruction (Corey et al. 1982)
0.2 ± 0.1 to 1.4 ± 0.9 (respirable) 0.1 ± 0.2 to 2.0 ± 2.0 (total)	Wheezing, rhinitis, sputum, eye irritation, cough, shortness of breath (Broder et al. 1985)
2.4 to 17.5 (total area) 8.3 to 25.3 (total personal)	Eye and nasal irritation, wheezing, cough, breathlessness, sputum production (Chan-Yeung et al. 1980)
5.4 to 6.3 (total area) 3.7 to 17.2 (total personal)	Eye and nasal irritation, wheezing, cough, breathlessness, sputum production (Chan-Yeung et al. 1981)

*Range or mean $\pm$ the standard deviation. A standard deviation may be larger than the mean because data are greatly skewed. Data are nonetheless valid.

5.7.1.1 doPico et al. (1977)

doPico et al. (1977) used the results of a November 1974 health survey to evaluate the health status of 300 grain elevator workers in Superior, Wisconsin, and Duluth, Minnesota, U.S.A. The number of candidates identified for the study was not stated. Some of the workers did not participate in the study because of scheduling conflicts or other personal reasons. No comparison population was included.

The workers were given a limited physical examination and were administered medical and occupational questionnaires to obtain information on respiratory symptoms, smoking habits, current and prior employment, and personal and family history of pulmonary and other diseases. Spirometric measurements were obtained for forced expiratory volume in 1 second (FEV_1), forced vital capacity (FVC), mean forced expiratory flow during the middle half of the FVC ($FEF_{25-75\%}$) (i.e., maximum mid-expiratory flow rate [MMF]), instantaneous maximal expiratory flows after exhalation of 50% and 75% of the FVC ($FEF_{50\%}$ and $FEF_{75\%}$), diffusion capacity of the lung for carbon monoxide (DL_{CO}), and closing volume (CV). Other tests included (1) posteroanterior chest radiographs, (2) venous blood samples for serum precipitin tests using grain dust, grain extracts, and mixed molds, (3) intradermal skin tests using extracts of rat hair, flax, pollen, alternaria, mixed grasses, mixed trees, and mixed insect parts, and (4) skin tests (by the prick method) using grain dust and extracts of barley, oats, and rye. Grain dust exposure data were collected 6 months before the study. Total dust concentrations ranged from 10.3 to 253 mg/m^3 of air as 8-hour time-weighted averages (8-hr TWA's). Sixty-six percent of the samples (60 of 91) exceeded 15 mg/m^3, the U.S. Occupational Safety and Health Administration (OSHA) permissible exposure limit (PEL) for total nuisance dust.

Results of the questionnaire indicated that upon exposure to grain dust, 77% of the workers complained of eye symptoms (e.g., eye burning, itching, scratching, and redness), 64% reported nasal symptoms (e.g., stuffiness and rhinorrhea), and 88.6% complained of one or more respiratory symptoms (e.g., coughing and wheezing). Coughing and wheezing were more common among workers who smoked than among those who did not ($p<0.025$). Compared with nonsmokers, smokers had a significantly higher rate of persistent cough ($p<0.005$), morning expectoration ($p=0.002$), chronic bronchitis ($p<0.01$), and wheezing ($p<0.01$).

Pulmonary function values for 298 grain workers were analyzed. Values for pulmonary function did not decrease noticeably when length of employment was adjusted for age and height. When comparing the relationship between symptoms and pulmonary function, a significant number of workers who reported wheezing had abnormal $FEF_{25-75\%}$ ($p<0.005$), FEV_1, $FEF_{50\%}$, and $FEF_{75\%}$ ($p<0.005$). A significant number of workers who reported cough, expectoration, wheezing, dyspnea, and chest tightness had abnormal $FEF_{25-75\%}$ ($p<0.05$) and $FEF_{75\%}$ ($p<0.01$). Wheezing and cutaneous reactivity to grain dust were positively correlated ($p<0.02$). Precipitin tests, skin tests, and chest radiographs produced no significant values.

5.7.1.2 doPico et al. (1984)

doPico et al. (1984) compared the respiratory parameters of worker populations with and without grain dust exposure. Both groups were located in Superior, Wisconsin, and Duluth, Minnesota, U.S.A. The study was conducted between 1978 and 1980 (months were not given). Candidates identified for the study included 397 workers with exposure to grain dust. Some of these workers did not subsequently participate in the study because of scheduling errors or personal reasons. The survey therefore included 310 grain workers and a comparison population of 239 city service workers. The comparison population did not differ significantly from the grain workers in age, sex, height, weight, or smoking habits.

The workers were given a limited physical examination and were administered medical and occupational questionnaires to obtain information on respiratory symptoms, smoking habits, current and prior employment, and personal and family history of pulmonary and other diseases. Spirometric measurements were obtained for FEV_1, FVC, $FEF_{25-75\%}$, $FEF_{50\%}$, $FEF_{75\%}$, DL_{CO}, CV, and the slope of Phase III of the alveolar plateau ($\Delta N_{2/L}$) (a measure of the intrapulmonary distribution and mixing of air). Values obtained were compared with published data on predicted normal values. Posterior and anterior chest radiographs were taken. No data were reported on grain dust concentrations.

Overall, grain workers had a statistically greater occurrence of respiratory symptoms ($p<0.001$), specifically wheezing and/or chest tightness ($p<0.001$). The prevalence of respiratory symptoms associated with smoking habits is shown for grain workers and service workers in Table III. A logistic regression analysis indicated an association between smoking and grain handling with chronic bronchitis and wheezing ($p<0.001$).

Spirometric data were evaluated for 310 grain workers and 237 comparison workers. The mean values for FEV_1, FVC, $FEF_{25-75\%}$, $FEF_{50\%}$, and

$FEF_{75\%}$ were significantly lower for the grain workers than for the city service workers ($p<0.05$). Airway obstruction as measured by FEV_1/FVC, $FEF_{25-75\%}$, and $FEF_{50\%}$ was more prevalent ($p<0.05$) for workers with chronic bronchitis than for those without. Regardless of smoking habits, airway obstruction as measured by FEV_1/FVC was more prevalent ($p<0.05$)

Table III.--Relationship of smoking habits to the prevalence of respiratory disorders or symptoms in grain workers and service workers*

		Percentage of workers with disorders or symptoms			
Disorder or symptom	Type of worker	All subjects	Smokers	Ex-smokers	Nonsmokers
Chronic bronchitis	G†	49§	57§	43§	35§
	C†	18	30	7	10
Expectoration	G	37§	46§	28§	29§
	C	15	26	4	8
Wheezing	G	65§	72§	58#	57#
	C	42	50	41	30
Dyspnea grade 1	G	38**	42#	32	37§
	C	27	30	36	11

*Adapted from doPico et al. (1984).
†G=grain workers, C=service workers.
§Significantly different from service workers ($p<0.005$).
#Significantly different from service workers ($p<0.05$).
**Significantly different from service workers ($p<0.01$).

in grain workers than in comparison workers.

A logistic regression analysis produced the odds ratios (i.e., the probability of having a symptom divided by the probability of not having the symptom) listed in Table IV. These ratios indicate that the odds of developing respiratory symptoms from grain dust exposure are independent of and usually greater than the odds of developing them from smoking.

5.7.1.3 doPico et al. (1983)

A year before publication of the 1978-80 health survey (doPico et al.

1984), doPico et al. (1983) used the data from the survey to examine the health effects of grain dust and their relationship to airborne dust concentrations. The study was conducted between September and December in Superior, Wisconsin, and Duluth, Minnesota, U.S.A. Subjects included

Table IV.--Probability of having a respiratory disorder or symptom*

Disorder or symptom	Odds ratio	
	Grain handlers regardless of smoking status	Smokers regardless of grain handling status
Chronic bronchitis	4.4	2.9
Wheezing at work	4.8	1.9
Wheezing at home	2.2	1.8
Airway obstruction	2.6	2.7

*Adapted from doPico et al. (1983).

283 grain elevator workers and 192 city service workers (comparison population). The two groups were comparable with respect to age, sex, height, weight, and smoking habits.

The workers were given a limited physical examination and were administered medical and occupational questionnaires to obtain information on the frequency of eye, nasal, and respiratory symptoms and their perceived level of dust exposure ("less than average," "above average," or "average"). Spirometric measurements were obtained for FVC, FEV_1, $FEF_{50\%}$, and $FEF_{75\%}$. Other tests included (1) oral temperature, (2) skin tests using pollen, mixed feathers, cat and rat epithelium, grass, and mixed grain dusts, and (3) venous blood samples for total leukocyte count. During the work shift, 209 total dust measurements (8-hr TWA's) were made. Ninety-three percent of the grain dust concentrations were below 10 mg/m^3, and 86% were below 5 mg/m^3, with a mean concentration of 3.3 mg/m^3.

Statistically significant differences ($p<0.05$) existed in the prevalence rates of the following symptoms among all grain workers and all comparison workers, respectively: cough, 48% and 32%; expectoration, 38% and 19%; wheezing, 13% and 9%; dyspnea, 12% and 6%; nasal stuffiness, 38% and 26%; and eye irritation, 13% and 6%. In the comparison group, workers who smoked had a significantly greater prevalence ($p<0.05$) of cough, expectoration, and nasal symptoms than did nonsmokers. Grain elevator workers who reported that their perceived exposure to grain dust was "average" had a significantly greater occurrence ($p<0.05$) of cough than those who reported "less than average" exposures. Those who assessed their exposure as "greater than average" had a significantly greater prevalence ($p<0.05$) of dyspnea, wheezing, and eye symptoms than those reporting "average" or "less than average" exposures.

An analysis of the relationship between dust concentrations and symptom prevalence was conducted for 209 grain workers (no explanation was given for the reduced number of workers). At total grain dust concentrations >5 mg/m^3, grain workers had a significantly greater prevalence of cough ($p<0.005$), expectoration ($p<0.0001$), dyspnea ($p<0.001$), and eye irritation ($p<0.0001$) than did city service workers.

An analysis of pulmonary function values for 241 grain workers and 191 comparison workers was conducted (no explanation was given for the reduced number of workers). Grain workers experienced a significant pre-shift to post-shift percentage change for FVC ($p<0.05$), $FEF_{50\%}$ ($p<0.01$), and $FEF_{75\%}$ ($p<0.001$). A multiple regression analysis correcting for age, height, and smoking habits revealed that the grain dust concentration had a statistically significant ($p<0.05$) effect on the pre-shift to post-shift percentage changes in FVC, $FEF_{50\%}$, and $FEF_{75\%}$. The significant effect noted for FVC limits the validity of the flow rate measurements, as the lung volume shifted the volume at which the flow measurements were made.

For grain workers, a significant correlation ($p<0.05$) existed between total dust concentration and the pre-shift to post-shift change in leukocyte count. No significant correlations occurred in serum precipitin tests. The general conclusion from the ventilatory function testing indicates that chronic exposure to grain dust did not produce a mean decrement in group function. However, an acute airway response to grain dust was demonstrated by pre- to post-shift response measurements. In addition, the correlation of irritant-induced symptoms (eye and nose irritation and cough) with ventilatory reduction convincingly indicates that grain dust contains an irritating, inflammatory substance or substances. No conclusions can be made regarding the influence of smoking.

5.7.2 Studies of workers in Thunder Bay, Saskatchewan, Canada

A series of reports has been published examining the prevalence, nature, and cause of respiratory disease of grain workers in Thunder Bay, Saskatchewan, Canada. Broder et al. (1979) reported on a May to August 1977 health survey of workers with and without exposure to grain dust. Corey et al. (1982) and Broder et al. (1983) reported the results of special tests and/or analyses performed by Broder et al. (1979) on subsets of these populations. A longitudinal study from December 1977 to June 1978 (Broder et al. 1980) reported changes in respiratory values for the Saskatchewan grain workers. Broder et al. (1985) reported on a May to August 1980 health survey of the same worker populations.

5.7.2.1 Broder et al. (1979)

Broder et al. (1979) used the results of a 1977 health survey to determine the prevalence of respiratory abnormalities in worker populations with and without exposure to grain dust. The number of candidates identified for the study is not clearly stated by the authors. Some workers did not participate in the study because of illness or other personal reasons. The initial survey included 441 grain elevator workers (identified in the report as workers from Wheat Pools 4 and 7) and a comparison population of 180 civic workers. Of the grain elevator workers, 189 were from Wheat Pool 4 and 252 were from Wheat Pool 7.

The workers were given a limited physical examination and were administered medical and occupational questionnaires to obtain information regarding the presence, duration, and frequency of eye, nasal, and respiratory symptoms and aggravating factors. Information was collected about current and prior employment, smoking history, and personal and family history of atopic disease.

Spirometric data were obtained from both worker groups. Measurements were obtained for the following ventilatory function tests: functional residual capacity (FRC), relaxed vital capacity (RVC), total lung capacity (TLC), residual volume (RV), FEV_1, $FEF_{50\%}$, instantaneous maximal expiratory flow after exhalation of 25% of the FVC ($FEF_{25\%}$), instantaneous maximal expiratory flow of 60% of TLC ($FEF_{60\%TLC}$), and DL_{CO}. The values obtained were compared with published data on predicted normal values. The grain workers and civic workers were similar in height, weight, and duration of employment; workers from both groups were matched for smoking habits. Other tests included (1) 35- x 43-cm posteroanterior chest radiographs, and (2) skin tests (by the scratch method) using mixed molds, grass, pollen, grain dust, house dust, and yeast. No values were reported for airborne grain dust concentrations.

For nonsmokers, the mean FEV_1 was $96 \pm 15\%$ of the predicted value (a reference [normal] value based on a single well-selected population) for workers in Wheat Pool 4 and $104 \pm 15\%$ of the predicted value ($p<0.05$) for comparison workers. The mean FEV_1 for workers in Wheat Pool 7 was not statistically different from that of the comparison workers. The frequency of a family history of asthma and positive skin reactions to molds or pollens was lower in the grain workers than in the comparison workers. This fact suggests a self-selection of non-atopic workers for chronic exposure. The frequency of cough, rales, and positive skin reactions to grain dust was higher in the grain workers than in the comparison group. No significant differences were observed between the chest radiographs of grain workers and those of the comparison group. Using a linear regression analysis where duration of employment was an independent variable, Broder et al. (1979) observed a decrement in ventilatory performance that could not be attributed to duration of employment at the grain-handling facility.

5.7.2.2 Corey et al. (1982)

In a report based on information collected in the 1977 survey (Broder et al. 1979), Corey et al. (1982) noted changes in ventilatory performance among a subset of workers. Candidates identified for the study included 47 grain elevator workers from Wheat Pool 4 and 15 civic workers (comparison population). Selection of study candidates was based on the feasibility of releasing them from their work duties.

The workers were given a limited physical examination and were administered medical and occupational questionnaires to obtain information regarding the presence, duration, and frequency of eye, nasal, and respiratory symptoms and aggravating factors. Information was collected about current and prior employment, smoking history, and personal and family history of atopic disease.

Spirometric data were obtained from both worker groups. Measurements were obtained for the following ventilatory function tests: FEV_1, FVC, $FEF_{50\%}$, $FEF_{25\%}$, FRC, TLC, and RV. Maximum expiratory flow volume curves for grain workers were ascertained at the beginning and end of the work shift on Monday, Wednesday, and Friday of a given week. Lung volumes were ascertained at the beginning of the work shift on Monday and at the end of the work shift on Friday. Ventilatory function measurements were taken on Monday and Friday mornings for the comparison group. Workers were monitored for respirable and nonrespirable dust during the full shift on all 5 days of the same test week. The average respirable dust concentration was 0.9 ± 0.7 mg/m^3, and the average nonrespirable dust concentration was 5.7 ± 10.9 mg/m^3. Note that the standard deviation for the nonrespirable dust concentration is larger than the mean because the data are greatly skewed; the validity of the data is not affected, however.

Pulmonary function analyses were based on results from 34 of the 47 grain elevator workers (the remaining 12 workers were either unable to report for the tests or had results that were rejected on technical grounds). The FVC decreased from Monday to Wednesday, and the Wednesday change was sustained on Friday ($p<0.001$). The FEV_1 and FEV_1/FVC decreased from Monday to Wednesday morning and the Wednesday decreases were sustained on Friday morning ($p<0.0001$). All values increased every afternoon with respect to the morning values of the same day ($p<0.0001$). A Monday morning to Friday morning decrease occurred for $FEF_{50\%}$ ($p<0.001$) and $FEF_{25\%}$ ($p<0.2$). A decrease in TLC also occurred from Monday to Friday afternoon ($p=0.05$). For the 15 civic workers, a significant decline occurred in $FEF_{50\%}$ ($p=0.03$) and $FEF_{25\%}$ ($p=0.05$) from Monday to Friday morning. For grain workers, the within-day decreases in $FEF_{50\%}$ and $FEF_{25\%}$ from Monday to Wednesday indicate airway obstruction, whereas the decline in TLC indicates volume restriction. For civic workers, the decreases in $FEF_{50\%}$ and $FEF_{25\%}$ indicate obstructive impairment without restriction.

These data were used to examine a dose-effect relationship for grain dust exposure. Results showed that 50% of the workers underwent a daily decrease of at least 923 ml/sec in $FEF_{50\%}$ (p=0.004) and of 310 ml/sec in $FEF_{25\%}$ (p=0.08) for each 1 mg/m^3 increase in the concentration of respirable dust.

5.7.2.3 Broder et al. (1983)

In a report based on information collected in the 1977 survey (Broder et al. 1979), Broder et al. (1983) studied possible airway obstruction and lung volume restriction in subsets of workers from 441 grain elevator workers and 179 civic workers.

The workers were given a limited physical examination and were administered medical and occupational questionnaires to obtain information regarding the presence, duration, and frequency of eye, nasal, and respiratory symptoms and aggravating factors. Information was collected on current and prior employment, smoking history, and personal and family history of atopic disease. Spirometric data were obtained from both worker groups. Other tests included (1) 35- x 43-cm posteroanterior chest radiographs, (2) skin tests (by the scratch method) at a strength of 1:10 weight/volume for mixed molds, mixed grass, mixed pollen, and mixed grain dust, house dust, and yeast, (3) inhalation challenge with methacholine, grain dust, grain dust extract, and potato starch, and (4) venous blood samples using serum precipitin tests for molds and α_1-antitrypsin. No values were reported for airborne grain dust concentrations.

No results were reported for the chest radiographs.

On the basis of skin tests results, two subsets of grain workers were established for further study: (1) 18 grain handlers with positive reactions to one or more grains and a comparison group of 18 grain workers with no reaction, and (2) 21 grain handlers with positive reactions to one or more fungal antigens and a comparison group of 21 grain workers with no reaction. Workers were matched for age, duration of employment, smoking status, and pack years of smoking. No significant differences were found for demographics, respiratory symptoms, or pulmonary function.

On the basis of results of the inhalation challenge tests, three subsets of grain workers were established for further analysis: (1) 12 nonsmoking grain workers with chronic cough and 12 grain workers with no cough (internal comparison group), (2) 9 grain workers with a decrease in $FEF_{50\%}$ from Monday to Friday and 9 grain workers with no decrease in $FEF_{50\%}$ (internal comparison group), and (3) 10 grain workers whose baseline FEV_1 was $\leq 70\%$ and 7 grain workers whose baseline was >100% (internal comparison group). Insofar as possible, the internal comparison workers were matched with the other grain workers for age, duration of employment, and smoking history. No significant differences were found for demographic variables, respiratory symptoms, or pulmonary function.

Serum precipitin tests were conducted on 441 grain handlers and 179 civic workers. The concentration of α_1-antitrypsin was significantly higher in grain workers than in the comparison group ($p<0.001$), but this result was interpreted by the authors as a possible indication of pulmonary inflammation.

The results of this study are inconclusive of a Type I (IgE-mediated) allergic reaction as the basis for pulmonary function changes seen in grain elevator workers.

5.7.2.4 Broder et al. (1980)

Broder et al. (1980) examined the longitudinal changes in the respiratory variables of the Saskatchewan grain workers. The study was conducted between December 1977 and June 1978; it was designed to determine how periods of layoff affected respiratory variables. From Saskatchewan Wheat Pool 4, 80 workers with the least seniority were selected for inclusion in the study. Seventy-seven of these workers chose to participate in the study.

The workers were administered medical and occupational questionnaires to obtain information regarding the presence, duration, and frequency of eye, nasal, and respiratory symptoms and aggravating factors. Information was collected about current and prior employment, smoking history, and personal and family history of atopic disease. Spirometric measurements were obtained for FVC, FEV_1, $FEF_{25\%}$, and $FEF_{50\%}$. Values obtained were compared with published data on predicted normal values. No samples were taken to determine airborne grain dust concentrations.

The 41 workers with the least seniority were laid off during the study period because of a lack of grain shipments. A short questionnaire was administered, and ventilatory performance tests were conducted monthly until the time of layoff. During the layoff period, workers filled out a brief questionnaire and underwent pulmonary function tests at monthly intervals. Not all workers participated in every monthly assessment. The assessments were conducted on the same half day of each week. The questions asked in followup assessments were oriented to cover the time period since the previous visit, and the same pulmonary function tests were performed each time. After the workers were rehired, they were examined monthly. The mean layoff duration was 82 days (range, 17 to 155 days).

For the longitudinal analysis, 14 workers who were laid off and 14 who were not laid off were matched as closely as possible for age and smoking habits. The laid-off workers were examined in January and February before being rehired; they were subsequently examined between April and June. Steadily employed workers were examined at the same intervals. After they were rehired, workers who had been laid off reported an increase in cough ($p<0.04$), rhinitis ($p<0.03$), and sputum production ($p<0.05$), and a decrease in shortness of breath ($p<0.01$) and respiratory illness ($p<0.02$). Workers who were steadily employed had an increase in cough ($p<0.04$), rhinitis ($p<0.03$), and sputum production ($p<0.05$) during the same time period. Compared with these workers, those who had been laid off reported significantly less cough ($p<0.05$) and sputum production ($p<0.01$) in February, and less shortness of breath ($p<0.05$) after they were rehired. Workers who had been laid off showed improvement in FEV_1 ($p<0.001$) and $FEF_{50\%}$ ($p<0.001$) in February followed by a decline after they were rehired. For that same period, steadily employed workers had an increase in FEV_1 ($p<0.002$) in February followed by a decline.

An analysis covering the maximum consecutive period of reduced employment (January to March) included 15 workers who were laid off and 24 steadily employed workers. The subjects were not matched for age or smoking habits. The steadily employed workers had a significant increase in cough ($p<0.02$) and sputum production ($p<0.001$).

Though low ambient temperature may have had an effect on the respiratory symptoms, adverse symptoms continued to increase as the temperature increased. The longitudinal changes in respiratory variables are partially reversible and are consistent with the effects of grain dust exposure.

5.7.2.5 Broder et al. (1985)

Broder et al. (1985) conducted a followup health survey on the 441 grain elevator workers and 180 civic workers from the initial 1977 health survey (Broder et al. 1979). Only 315 grain workers and 107 civic workers were available, since the remainder had retired, left their jobs, or did not report for their appointments. The results from this 1980 health survey were compared with those obtained from the 1977 health survey (Broder et al. 1979). Both surveys were conducted from May to August.

Workers were given a limited physical examination and were administered medical and occupational questionnaires. Information was solicited on the occurrence of symptoms, smoking history, occupational history, past illnesses, allergic problems, and family history of respiratory and allergic conditions.

Spirometric data were obtained from both worker groups. Measurements were determined for FEV_1, FVC, $FEF_{50\%}$, and $FEF_{75\%}$. Area samples were collected for respirable and nonrespirable grain dust. The respirable fraction ranged from 0.2 ± 0.1 to 1.4 ± 0.9 mg/m^3. The nonrespirable fraction ranged from 0.1 ± 0.2 to 2.0 ± 2.0 mg/m^3. Because of improvements in engineering controls at the facilities, the concentrations of dust were lower than those measured during the initial health survey.

Data obtained in the 1977 survey (Broder et al. 1979) for the grain and civic workers who left employment before the 1980 survey were compared with data obtained from those workers who remained employed and were reexamined in 1980 (Broder et al. 1985). The grain handlers who had left employment were significantly younger ($p<0.001$), had a shorter duration of employment ($p<0.001$), and reported a greater prevalence of eye irritation ($p<0.04$), cough ($p<0.04$), and shortness of breath ($p<0.003$) than those grain workers who remained employed. The groups were compared using multiple logistic analyses of the symptoms and multiple regression analyses of pulmonary function measurements with adjustments for age, pack years of smoking history, and duration of employment. These adjustments increased the differences in prevalence rates for the aforementioned symptoms but they did not change the statistical significance. The adjustments also increased the significance of the reported sputum prevalence from $p=0.04$ to $p<0.02$. Civic workers who left the job were significantly younger ($p<0.001$), had a shorter duration of employment ($p<0.002$), had decreased pack years of smoking history ($p<0.001$), included a lower percentage of current smokers ($p<0.02$), had a lower prevalence of coughing ($p<0.02$), and had a lower FVC ($p<0.002$), a higher FEV_1/FVC ratio ($p<0.02$), and a higher $FEF_{75\%}$ ($p<0.005$) than those civic workers who remained employed. When adjusted for age, pack years of smoking history, and duration of employment, the differences were no longer statistically significant.

Data obtained in the 1977 survey (Broder et al. 1979) for the grain and civic workers who remained employed and were reexamined were compared with data obtained from those workers who remained employed but did not report for the 1980 survey (Broder et al. 1985). The grain workers who declined participation in the 1980 survey were significantly older ($p<0.007$), had a longer duration of employment ($p<0.009$), and had a greater number of pack years of smoking history ($p<0.006$) when compared with those grain workers who were reexamined in the 1980 survey. The grain workers who declined participation in the 1980 survey had a higher prevalence of sputum production ($p<0.01$), lower FEF_{50} ($p<0.009$), and FEV_1/FVC ($p<0.006$) when compared with those grain workers who were reexamined in the 1980 survey. However, the significance for these pulmonary parameters declined when adjusted for number of pack years of smoking. The civic workers who declined to participate in the 1980 survey were significantly older ($p<0.03$) than those civic workers who were reexamined.

There was a statistically significant greater prevalence of wheezing in nonsmoking civic workers compared with nonsmoking grain workers in 1977 ($p<0.03$) and in 1980 ($p<0.001$). In 1977, increased eye irritation ($p<0.01$) and a higher $FEF_{75\%}$ ($p<0.02$) was measured in grain workers who smoked compared with civic workers who smoked. For grain and civic workers whose smoking status remained constant from 1977-80, Table V shows demographic characteristics, symptom prevalence, and measures of pulmonary function.

Table V.--Characteristics of grain and civic workers whose smoking status remained constant*

Item	Nonsmokers				Ex-smokers				Current smokers			
	Grain		Civic		Grain		Civic		Grain		Civic	
	1977	1980	1977	1980	1977	1980	1977	1980	1977	1980	1977	1980
Characteristics of workers:												
Number	44	44	22	22	88	88	26	26	141	141	46	46
Avg age	35	38†	38	41†	43	46†	47	50†	38	41	41	44†
Avg pack years	0	0	0	0	23	23	22	22	24	28†	25	29§
Avg years employed	9	12†	9	12†	15	18†	14	17†	11	14†	11	14†
Symptoms (avg. %):												
Sputum	11	16	5	9	17	15	15	19	47	60†	50	59
Wheeze	2	0	18	23	17	14	4	4	23	30	24	35
Rhinitis	16	14	32	18	26	19	23	27	33	25§	33	35
Eye irritation	25	18	14	9	24	15	12	19	25	18	7	9
Measure of pulmonary function (avg. % predicted)												
FVC (L)	4.94	4.83	5.15	5.10	4.77	4.69#	4.74	4.69	4.88	4.76†	5.05	4.93#
FEV_1 (L/sec)	3.39	3.91	4.08	4.05	3.56	3.59	3.57	3.50§	3.61	3.60	3.66	3.71
FEV/FVC	0.80	0.81	0.79	0.80	0.74	0.76	0.76	0.76	0.74	0.75	0.73	0.75
$FEF_{50\%}$ (L/sec)	5.67	5.38	5.31	5.16	4.94	4.70†	4.46	4.18	4.66	4.45	4.26	4.39
$FEF_{75\%}$ (L/sec)	2.2	2.04	1.93	1.79	1.49	1.48	1.26	1.18	1.61	1.43†	1.27	1.41

*Adapted from Broder et al. (1985).
†Statistically different from 1977 ($p<0.001$).
§Statistically different from 1977 ($p<0.05$).
#Statistically different from 1977 ($p<0.01$).

The changes in pulmonary function from 1977 to 1980 show (1) a significant increase in FEV_1/FVC ($p<0.04$) among grain workers who were ex-smokers compared with civic workers who were ex-smokers, and (2) a decline in $FEF_{75\%}$ ($p<0.002$) among grain workers who were current smokers compared with civic workers who were current smokers. A multiple regression analysis of change in pulmonary function from 1977 to 1980 demonstrated an inverse relationship between age in 1980 and the level of pulmonary function in 1977.

The longitudinal study by Broder (1980) showed that there was an increased prevalence of rhinitis, cough, and sputum production among rehired grain workers compared with continuously employed grain workers. However, the rehired workers showed a decrease in the prevalence of shortness of breath and respiratory illness compared with the continuously employed grain workers. This result may indicate that continuously employed grain workers are at greater risk for chronic inflammatory disease. The decreases in ventilatory function noted from Monday to Friday by Corey et al. (1982) indicated chronic pulmonary obstruction (flow) and restriction (volume).

The studies reported by Broder et al. indicate changes in pulmonary function over time that did not exceed expectations. However, the selective factors for both initial and continued employment in this industry could influence the pulmonary function results observed in grain workers. Some refer to the influence of these selective factors as the "healthy worker effect." Those workers who are healthy initially are hired as grain workers and those who subsequently suffer the fewest respiratory symptoms remain employed as grain workers. If these selective factors affect the number and types of symptoms reported by grain workers, then comparison with workers who are not subject to the selective forces may understate the potential effects of grain dust.

5.7.3 Studies of workers in Vancouver, British Columbia, Canada

A series of reports have been published examining the prevalence, nature, and cause of respiratory disease of grain workers in Vancouver, British Columbia, Canada. Chan-Yeung et al. (1980) reported on an October 1975 to June 1977 health survey of grain workers. Chan-Yeung et al. (1981) reported on a 1978-80 health survey (months not given) of grain workers and a comparison population. Tabona et al. (1984) reported on an October to November 1981 health survey of these same populations. Chan-Yeung et al. (1979) reported the results of special tests and/or analyses performed by Chan-Yeung et al. (1980) on subsets of these populations. Enarson et al. (1985) reported the results of special tests and/or analyses performed by Tabona et al. (1984) on subsets of these populations. These reports followed portions of the same populations of grain workers and controls for periods as long as 6 years (Table VI). For the first health survey, workers were selected from four grain elevators in the Port of Vancouver and from one grain elevator in Prince Rupert. Subsequent studies examined only those workers from the four Port of Vancouver elevators.

Table VI.--Summary of five reports on grain workers in British Columbia

Report	Survey period	Workers evaluated
1. Chan-Yeung et al. (1980)	1975-77	610 grain workers 136 civic workers 187 sawmill workers
2. Chan-Yeung et al. (1979)*	1975-77	33 grain workers
3. Chan-Yeung et al. (1981)	1978-80	396 grain workers 111 civic workers
4. Tabona et al. (1984)	1981	267 grain workers
5. Enarson et al. (1985)	1981	81 grain workers

*Note that this report was published before the report on which it was based (Chan-Yeung et al. 1980).

5.7.3.1 Chan-Yeung et al. (1980)

Chan-Yeung et al. (1980) described the results of a health survey in which the prevalence of respiratory symptoms was determined among workers exposed to grain dust. The study was conducted between October 1975 and June 1977. Candidates identified for study included 642 workers from five grain elevators, 206 civic workers, and 302 noncedar sawmill workers (1980). Because there were no female grain elevator workers, women were excluded from the two comparison populations. Nonwhite workers were eliminated

Table VII.--Characteristics of grain, civic, and noncedar sawmill workers[*]

Characteristics	Grain workers		Civic workers		Sawmill workers	
	Number	%	Number	%	Number	%
No. of workers	610	---	136	---	187	---
Age, years (mean±SD)	37.8±12.6	---	44.3±11.2[†]	---	43.1±13.8[†]	---
Duration of employment, months (mean±SD)	102.6±92.9	---	151.9±127.7[†]	---	186.7±128.5[†]	---
Smoking habits:						
Nonsmokers	130	21.2	42	30.9[§]	30	16.0
Ex-smokers	180	29.5	54	39.7[§]	66	35.3
Current smokers	300	49.2	40	29.4[§]	91	48.7

[*]Adapted from Chan-Yeung et al. (1980).
[†]Significantly different from grain workers ($p<0.05$).
[§]Significantly different from grain workers and sawmill workers ($p<0.05$).

because of differences in predicted pulmonary function values. In addition, some workers were excluded because of prior exposure to red cedar dust (a recognized respiratory tract irritant). The initial survey therefore involved 610 grain elevator workers and comparison populations of 136 civic workers and 187 sawmill workers (Table VII).

The workers were administered medical and occupational questionnaires to obtain information regarding the occurrence of eye, nasal, and respiratory symptoms that occurred during work hours and on weekends or holidays and that were associated with smoking habits. Information was also collected about current and prior employment, and personal and family history of atopic disease.

Spirometric data were obtained from all worker groups. Measurements of FEV_1 and FVC were used to calculate $FEF_{25-75\%}$, and the values obtained were compared with published data on predicted normal values. The data were adjusted for age and height and analyzed for the effects of work, smoking, duration of employment, and the interactions of these factors using standard methods for the analysis of covariance. Other tests included (1) 14- x 17-in. posteroanterior chest radiographs, (2) skin tests (prick method) using grain elevator dust, house dust storage mite (D. farinae), mixed molds, and mixed Pacific grass pollen, and (3) determination of serum α_1-antitrypsin.

Personal and area air samples for total dust were obtained during 8-hr periods in all five grain elevators and in the sawmills. In the grain elevators, area dust concentrations ranged from 2.4 to 17.6 mg/m^3, and personal samples ranged from 8.3 to 25.3 mg/m^3. For the five elevators, the crystalline silica content of the dust ranged from 3.8% to 5.0%. The average total dust concentration in the sawmills was 1.9 mg/m^3 (the range was not reported).

There were no statistically significant differences between grain workers and civic workers with regard to the prevalences of eye, nasal, and chest symptoms when workers were matched for smoking habits. Grain workers and sawmill workers had statistically significant differences in the prevalences of these symptoms (Table VIII). Cough, sputum, wheezing, and breathlessness were more prevalent in smokers than in nonsmokers in all

Table VIII.--Prevalence rates for eye, nasal, and chest symptoms in grain, civic, and sawmill workers[*]

Smoking status	Type of worker		Prevalence rate (mean %): Eye symptoms	Nasal symptoms	Cough	Sputum	Wheezing	Breathlessness
Nonsmoker	G[†]	130	29[§]	28	20	18	20[#]	18
	C[†]	40	25	30	13	6	22	14
	S[†]	89	3	29	10	8	1	10
Ex-smoker	G	180	26[#]	34[§]	23	26[#]	24	24
	C	54	20	26	18	16	20	16
	S	66	10	9	9	6	8	19
Current smoker	G	300	26[§]	38[§]	50[§]	44[§]	42[§]	40[§]
	C	42	9	30	38	43	37	37
	S	30	6	20	26	24	10	19

[*]Data derived from Chan-Yeung et al. (1980).
[†]G=grain workers, C=civic workers, and S=sawmill workers.
[§]Significantly different from sawmill workers ($p<0.01$).
[#]Significantly different from sawmill workers ($p<0.05$).

groups. The predicted values for FEV_1 and FVC (mean percentage) were significantly lower for nonsmoking or ex-smoking grain workers than for nonsmoking or ex-smoking civic or sawmill workers ($p<0.05$). The more non-atopic status of grain workers compared with civic workers suggests that a self selection (healthy worker effect) occurs.

On three separate occasions during a workweek, spirometric data were obtained from 485 workers at the four grain elevators in the Port of Vancouver and from 65 workers at one of the noncedar sawmills. The first test (initial test) was conducted before the beginning of the first work shift of the week (day 1); the second test was conducted at the end of the first work shift (day 1); and the final test was conducted at the end of the last work shift of the week (day 5). At the end of day 1, grain workers had significantly lower FEV_1 ($p<0.05$) and FVC ($p<0.01$) values than those recorded before the shift began (initial test). For sawmill workers, however, the end-of-shift values for day 1 were significantly higher ($p<0.05$) than the initial values. At the end of the workweek (day 5), FEV_1 and FVC values for grain workers had decreased further and were significantly lower ($p<0.01$) than the initial values, whereas FEV_1 and FVC values for the sawmill workers increased and were significantly higher ($p<0.01$) than the initial values. It is unclear why the sawmill workers had increases in respiratory function values over a workweek.

5.7.3.2 Chan-Yeung et al. (1979)

In a report based on information collected in the 1975-77 health survey, Chan-Yeung et al. (1980) and Chan-Yeung et al. (1979) further evaluated 33 of the grain workers (Table IX). In addition to tests conducted in the primary study, other tests performed were (1) methacholine broncochallenge tests, with FEV_1 and FVC measured before and after the tests, (2) serum precipitin responses to grain dust extracts, (3) bronchial inhalation challenge to grain dust and grain dust extract, with FEV_1 and FVC measured before and after the tests, and (4) venous blood samples for determination of absolute eosinophil counts. On the basis of these test results, the 33 workers were divided into three groups. Twenty-two of these workers (Groups A and B) reported respiratory symptoms (cough, sputum production with or without wheezing, and breathlessness) and demonstrated decrements in lung function. Group A consisted of 6 workers who also had a

Table IX.--Characteristics of grain workers*

Characteristics	Group A†	Group B§	Group C#
No. of workers	6	16	11
Age (mean years±SD)	52±9.4	51.2±8.8	40±10.7
Duration of symptoms (mean years±SD)	6.4±4.8	7.5±5.5	---

*Adapted from Chan-Yeung et al. (1979).
†Workers who developed bronchial reaction to grain dust.
§Workers who showed no reaction to grain dust or grain dust extract challenge.
#Workers with no respiratory symptoms or lung function abnormalities.

bronchial reaction to an inhalation challenge of grain dust extract as indicated by a decrease in FEV_1 of greater than 20% from the control value (saline challenge). Group B consisted of 16 workers with no bronchial reaction to the grain dust extract inhalation challenge. Eleven grain workers who reported no respiratory symptoms were selected for a comparison population (Group C). Bronchial reactivity to methacholine in grain workers is shown in Table X. All 6 workers in Group A and 5 of

Table X.--Results of pulmonary function tests in grain workers following methacholine inhalation challenge*

Tests	Group A	Group B	Group C
FEV_1 (mean % of predicted ±SD)	63.7±10.8	72.6±17.1	116±7.6
$FEF_{25-75\%}$ (mean % of predicted ±SD)	32.3±10	38±14.5	105±18
FEV_1/VC (mean % of predicted ±SD)	59.3±5.5	58.3±8.3	78.9±4.7
PC_{20} mg/ml† (mean % of predicted ±SD)	0.36±0.34	4.87±6.88	>25

*Adapted from Chan-Yeung et al. (1979).
†PC_{20}=provocation concentration of methacholine to induce a 20% fall in FEV_1.

the 16 workers in Group B demonstrated bronchial reactivity to methacholine at a level similar to that of patients with symptomatic occupational asthma. The remaining workers in Group B showed bronchial reactivity to methacholine challenge within the range seen in patients with chronic bronchitis. Groups A and B had evidence of airway obstruction, indicated by the decline in FEV_1, $FEF_{25-75\%}$, and FEV_1/VC (Table X). Group A had an absolute eosinophil count of $244/mm^3$ compared with $156/mm^3$ for Group B. None of the subjects reacted to skin tests or responded to grain dust extracts with serum precipitins. Although grain dust did not cause a bronchial reaction in all the workers, it cannot be excluded as the causative agent for the asthma and chronic bronchitis. Asthma is not a graded uniform response across exposed groups; rather it is an incident frequency response. Also, the results of exposure to the settled grain dust may not be indicative of those that may occur with fresh grain dust.

5.7.3.3 Chan-Yeung et al. (1981)

Chan-Yeung et al. (1981) conducted a followup respiratory survey between 1978 and 1980 on 587 grain workers and a comparison population of 111 civic workers. The results from this study were compared with those obtained from the 1975-78 survey (Chan-Yeung et al. 1980). The civic workers were surveyed in January 1980. Medical and occupational questionnaires were administered to workers. Information was solicited on the occurrence of symptoms and questions were asked about current and prior employment, and personal and family history of atopic disease.

Spirometric data were obtained from all work groups. Measurements for the grain workers were conducted during the last work shift of the week (day 5), and those for the comparison population were conducted midweek. Measurements for FEV_1 and FVC were determined, $FEF_{25-75\%}$ was calculated, and all were compared with published data on predicted normal values. For grain workers, skin tests (by the prick method) were conducted for reaction to mixed Pacific grass pollen, mixed Pacific weed pollen, and cat fur. Civic workers were tested for skin reactions to D.farinae and mixed molds in the initial survey, but they were not retested. Area samples for total airborne grain dust concentrations ranged from 5.4 to 6.3 mg/m^3, and personal samples for total airborne grain dust concentrations ranged from 3.7 to 17.2 mg/m^3. Except for Elevator 4, the total dust concentrations were lower during this survey than during the initial survey.

In this survey, the prevalence of chest symptoms and the lung function findings were similar to the initial survey, except that breathlessness correlated significantly with age (p=0.02). A longitudinal analysis was conducted on 396 of the 587 grain workers and 111 civic workers who had participated in the original survey. Grain workers who smoked at the time of both surveys had a statistically significant increase in the prevalence of breathlessness ($p<0.05$). Grain workers who smoked at the time of the 1975-78 survey but who did not smoke at the time of the 1978-80 survey had a statistically significant decrease ($p<0.05$) in coughing and sputum production. In the 1978-80 survey, grain workers above age 50 had a statistically significant ($p<0.05$) decline in FEV_1 regardless of smoking habits. Grain workers above age 50 who smoked had a statistically significant ($p<0.05$) decline in $FEF_{25-75\%}$. The annual decline in lung function was not dependent on the initial lung function, presence of respiratory symptoms, atopic status, or duration of employment. A significant correlation existed (p=0.037) between annual changes in lung function and the acute changes in lung function over a workweek reported in the 1975-78 survey for grain workers. Because the surveys were conducted at different times of the year, variations in environmental conditions (e.g., temperature, humidity, and exposures) may have affected the results.

5.7.3.4 Tabona et al. (1984)

In the fourth report of the series, Tabona et al. (1984) conducted a health survey in October and November 1981 using workers from the same worker populations studied in the first three reports (Chan-Yeung et al. 1980, 1979, 1981). The characteristics of 267 grain workers who had not changed their smoking habits over the 6-year study period were compared with the characteristics reported in the first health survey (Chan-Yeung et al. 1980). Medical and occupational questionnaires were administered to workers. Questions were also asked about current and prior employment, timing of symptoms in relation to presence at and absence from work, and detailed smoking histories.

Spirometric measurements were obtained during the last work shift of the week (day 5) and were compared with day 5 measurements from the initial survey. Measurements of FEV_1 and FVC were determined, $FEF_{25-75\%}$ was calculated, and all were compared with published data on predicted normal values. Other tests included (1) skin tests for reaction to grass pollen, D. farinae, and cat epidermal antigen, with histamine as a positive control and saline as a negative control, and (2) methacholine inhalation challenge tests with FEV_1 and FVC measured before and after the tests. No gravimetric measurements of grain dust exposure were reported.

Analysis of covariance was conducted to study the effects of age and smoking. Age was directly correlated with longitudinal decrements in FEV_1 ($p<0.0001$), $FEV_{25-75\%}$ ($p<0.0001$), and FVC ($p<0.03$). Workers above age 50 had greater decrements in pulmonary function parameters than workers below age 30 in all smoking categories. The methacholine challenge test was defined as a PC_{20} of ≤ 8 mg/ml (concentration of methacholine needed to induce a 20% decrease in FEV_1). Responses to methacholine challenge were significant for FVC and $FEF_{25-75\%}$ in current smokers, for FEV_1 in ex-smokers ($p<0.05$), and for FEV_1 in current smokers ($p<0.01$). No correlation existed between symptom prevalence, sensitivity to common allergens, or initial lung function and longitudinal decline in lung function measurements. Regression analysis revealed a significant correlation between spirometry results over one workweek and longitudinal decline in spirometry results for FVC and $FEF_{25-75\%}$.

5.7.3.5 Enarson et al. (1985)

In the fifth report, Enarson et al. (1985) analyzed the respiratory functions of 81 of the grain workers described by Tabona et al. (1984). These workers were matched for age and smoking habits. Twenty-seven of the 81 (or the 10% of the original Tabona cohort with the worst trends in FEV_1) were designated as "cases." The 54 comparison grain workers were those of the original cohort with the best trends in FEV_1 during the study period. The following measurements of ventilatory function were obtained: FEV_1, FVC, and $FEF_{25-75\%}$. The cases demonstrated an average FEV_1 decline of >100 ml/year (a decrease of 682 ± 272 ml by 1981 from the original value of $3{,}806 \pm 935$ ml in 1975). Exposure to grain dust and the risk of developing decreased pulmonary function were evaluated qualitatively by occupational group. Workers were divided into three job categories: cleaner/sweeper, maintenance, and other. Workers were compared according to current job, usual job, and jobs ever held in the past. By comparing the distribution of cases and comparison workers in various job categories, the investigators calculated a dose-response curve correlating the airborne dust concentration and the odds ratio of being a case. The authors concluded that FEV_1 would not decrease at airborne dust concentrations below approximately 5 mg/m^3.

The reports demonstrated (1) acute airway responses (pre- to post-shift study) and a further decrement in response as the week progressed, (2) increased nonspecific airway responsiveness (methacholine challenge) and specific airway responsiveness (grain dust extract challenge), (3) an elevated eosinophil count indicative of allergic response, and (4) a correlation between annual change in lung function and acute responses (over the workweek) indicating progressive chronic debilitation. No conclusion could be made regarding the effects of smoking, but nonspecific bronchial hyperactivity was demonstrated by the methacholine challenge.

6. ANIMAL STUDIES

The animal studies cited here identify the mechanism(s) of lung response to grain dust exposure. Mice exposed to grain dust concentrations ranging from 1200 ± 500 to 5400 ± 700 mg/m^3 total dust for 2 to 28 days developed an increased pulmonary macrophage response (Armanious et al. 1982). Rabbits exposed to grain dust at 20 mg/m^3 for 24 weeks, 5 days a week, developed inflammation of the alveoli and interstitium (Stepner et al. 1986). Exposure to mycotoxin produced noncytotoxic histamine release in rat peritoneal cells (Warren and Holford-Stevens 1986) and inhibited several critical cellular functions in rat alveolar macrophages (Sorenson et al. 1986). In rats, intratracheal instillation of grain dust initiated an acute inflammatory reaction as evidenced by an influx of neutrophils into the airspaces and later into the lung interstitium (Keller et al. 1987). Rats do not respond to histamine, yet histamine is the major pharmacologic mediator of acute bronchoconstriction in man. The allergic anaphylactic response of guinea pigs is mediated by a subtype of IgG (heterocytrotropic IgG) which is unlike the human IgG mediated responses. Human allergy is IgE mediated (Bass et al. 1988).

Limited conclusions have been drawn from the rodent animal modeling studies of human etiopathogenes. However, these studies support the proposed immunologic mechanism(s) presented in this document.

7. POSSIBLE MECHANISMS OF ACTION

Grain dust is a complex mixture of organic and inorganic compounds. Investigators have not yet determined whether the various grain dusts themselves cause the respiratory responses or whether the contaminants of the dust initiate the reaction. Factors such as age, smoking habits, length of employment, and job category may also play a role in inducing respiratory disease (Flaherty 1982).

7.1 Allergic Response

Results have varied from studies of grain workers tested for allergic reactions to fungi. Lewis et al. (1986) conducted a radioallergosorbent test (RAST) on serum collected from grain workers (NIOSH 1986b) who had been skin-tested by the "prick" method with common extracts of airborne grain dust. Lewis et al. confirmed the use of aqueous extracts of grain dust as a source of material for the RAST assay, and found that the prevalence of IgE antibodies to grain dust antigens was significantly higher than the prevalence of IgE antibodies to grain antigens. In Sweden, febrile reactions occurred in 19% of farmers exposed to unusually moldy grain (Malmberg et al. 1985). This variability of the agents in dust may be partially responsible for the variations in hypersensitivity noted in the reports cited above; or other causal mechanisms may be involved such as irritant effects or toxic reactions (e.g., activation of the alternative pathway of complement activation).

Allergic reactions to grain mites and weevils have been described. Ingram et al. (1979) obtained responses to bronchial provocation after farmers inhaled storage mite extract. Warren et al. (1983) demonstrated an allergic response to the Canadian storage mite, <u>Lepidoglyphus destructor</u>, in a grain worker and in 12 of 100 asthmatic individuals by skin testing and inhalation challenge. Lunn and Hughes (1968) described a subject who developed an asthmatic response followed by an Arthus-type reaction after exposure to a 1% weevil extract.

7.2 Complement

The complement system is the primary humoral mediator of antigen-antibody reactions and is composed of at least 15 serum proteins that are capable of reacting with each other, with antibodies, and with cell membranes. These interactions lead to a variety of biological events ranging from lysis of cells, bacteria, and viruses to direct mediation of inflammatory processes. Also, complement can induce (1) other cellular and humoral effector systems, (2) histamine release from mast cells, (3) phagocytosis, (4) direct migration of leukocytes, and (5) the release of lysosomal constituents from phagocytes. The complement system functions through two pathways that are referred to as the classical and the alternative. The classical complement pathway may be activated immunologically by antigen-antibody complexes and by aggregated immunoglobulins, or it may be activated nonimmunologically by a number of chemically diverse substances (e.g., DNA, C-reactive protein, and trypsin-like enzymes) (Cooper 1978). The alternative complement pathway may be activated non-immunologically by aggregated immunoglobins, such as IgA, IgG4, and IgE molecules or by complex polysaccharides, lipopolysaccharides, or trypsin-like enzymes (Boackle 1986). Olenchock et al. (1978, 1980a, 1980b) and Olenchock and Major (1979) have suggested that grain dust induces activation of the alternative complement pathway in man and that the activity appears to vary depending on the type of grain dust exposure. Though a number of potential mechanisms or interactions have been activated [Wirtz et al. 1984b] the specific grain dust component that activates the alternative complement pathway is yet to be identified. Moldy hay has been shown to induce activation of the alternative pathway in human (Edwards 1976) and rabbit serum (Edwards et al. 1974).

7.3 Microbial Toxins

Bacteria are ubiquitous in grain dust (Dutkiewicz 1978; DeLucca et al.1984; Lacey 1980). Bacterial endotoxins are lipopolysaccharide-protein complexes of cell-wall components of gram-negative bacteria. Endotoxins are inflammatory agents that cause increased capillary permeability and cellular injury. Endotoxins have been found in airborne grain dust

(Olenchock et al 1978; Wirtz et al 1984b) as well as in settled dust. DeLucca and Palmgren (1987) reported a seasonal variation in endotoxin concentration in both respirable and settled grain dust. Endotoxin levels in settled dusts were lowest in January and highest in November. Respirable samples collected in the fall months (September and October) showed significantly higher levels than those collected on other sampling dates.

Mycotoxins such as aflatoxin are commonly found in grain. They are considered to be carcinogenic as well as hepatotoxic (WHO 1979). Mycotoxins are products of secondary fungal metabolism; they may be located within the hyphae and spores and may be excreted into the grain (Palmgren and Lee 1986). Mycotoxins are usually associated with a toxic reaction that occurs as a result of food ingestion. Burg and Shotwell (1984) measured the aflatoxin level of corn dust during harvest at a farm in Georgia, U.S.A., where the level of contamination was known to be high. Airborne dust samples collected at the front of the combine had an average aflatoxin concentration of 3,850 ng/g, and the operator was exposed to aflatoxin concentrations up to 1,360 ng/g in the combine cab. Sorenson et al. (1981) analyzed samples of airborne grain dust for aflatoxin. Samples were collected from grain terminals in Duluth, Minnesota, Superior, Wisconsin, and from a corn dumping station in Georgia. No aflatoxin was detected in the samples from the Superior-Duluth area, but the airborne corn dust from Georgia contained 130 ppb aflatoxin B_1. Dashek et al. (1983) later confirmed the absence of aflatoxin in grain from the Superior-Duluth area.

8. RESEARCH NEEDS

Research is needed in the following areas:

(1) Establish the relationship between the recognized health effects of exposure to grain dust and the various constituents of the dust, including the possible effects of pesticides, fumigants, endotoxins, and mycotoxins.

(2) Determine the relationship between the various acute and chronic clinical effects of grain dust exposure.

(3) Identify the importance of the host factor in modifying the workers' response to grain dust exposure.

(4) Determine the relationship between levels of grain dust exposure, smoking, and respiratory disorders.

(5) Determine the role and mechanism of action of grain dust components.

(6) Develop animal modeling studies to assess etiopathogenic and immunologic mechanisms for both dust-containing agents and host-mediated agents. Animal modeling studies could also indicate whether acute responders become chronically debilitated.

(7) Determine the feasibility and efficacy of using small amounts of mineral oil to reduce grain dust in elevators.

9. CONCLUSIONS

From epidemiologic studies it is evident that grain dust is associated with respiratory symptoms (i.e., cough, dyspnea, rhinitis, wheezing, and chronic airway obstruction) and nonpulmonary disorders (i.e., conjunctivitis, grain fever, and dermatitis). Epidemiologic data indicate an excess risk of chronic obstructive and restrictive pulmonary disease in workers with chronic exposure to grain dust, although the mechanism(s) responsible for the lung abnormalities is not known. Worker exposure to grain dust has resulted in increased incidences of chronic bronchitis, asthma and chronic obstructive pulmonary disease. These adverse health effects are likely to result from repetitive acute inflammatory responses to grain dust exposure.

Epidemiologic and animal studies support the hypothesis that immunologic mechanism(s) cause the adverse health effects seen in grain workers. Although thorough characterization of allergenicity (Type I [IgE-mediated]) is lacking, it can be concluded that potent immunologic responses evoke inflammatory-mediated responses in airway smooth muscle.

A number of animal studies have been conducted to examine the mechanisms of response to grain dust, but the modeling approaches taken do not study the same physiologic parameter of response. For instance, all human studies evaluate forced expiratory flowrate (FEV, FVC, $FEF_{25-75\%}$, yet the animal studies cited do not evaluate these parameters. If they did, it would be possible to compare animal and human responses almost directly.

Because exposure to grain dust results in an immunologic response in some individuals, it is presently impossible to recommend an exposure concentration at which all workers would be protected from adverse health effects. However, reducing exposure to grain dust will decrease exposure to the agent(s) in grain dust that elicit the adverse health effects. Preemployment medical screening (i.e., flow/volume ventilatory function test and methacholine challenge) should be used to counsel workers about their predisposition to adverse respiratory symptoms.

10. SUMMARY

Exposure to grain dust produces asthma, other respiratory effects (e.g., cough, rhinitis, and farmers lung), and nonpulmonary disorders (e.g., conjunctivitis, grain fever, and dermatitis). Though thorough characterization of allergenicity (Type I, IgE-mediated) is lacking, occupational exposure to grain dust has clearly been associated with potent systemic immunologic responses that evoke inflammatory responses of smooth muscle in the airways.

Key words: Grain dust, cough, wheezing, asthma, chronic bronchitis, farmer's lung, obstruction, restriction, rhinitis, and grain fever.