

OCCUPATIONAL RESPIRATORY DISEASES  
RELATED TO VEGETABLE AND OTHER NATURAL DUSTS

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L'Institut National pour la Sécurité Occupationnelle  
et la Santé des Ouvriers



A Monograph on:

OCCUPATIONAL RESPIRATORY DISEASES

RELATED TO VEGETABLE AND OTHER NATURAL DUSTS

This publication represents the views and expert opinions  
of a an international working group which met  
in Morgantown, West Virginia, USA,

25-29 April 1983

World Health Organization  
Organization Mondiale de la Santé

and

National Institute for Occupational Safety and Health

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This volume reviews the major work-related respiratory diseases in exposure to vegetable and other natural dusts; it points to gaps in knowledge requiring further investigation, advises on best known control measures and provides guidance to research methods that are feasible to undertake in both developing and highly industrialized countries. Most of the chapters ~~contained were reviewed by a joint NIOSH/WHO workshop in Morgantown, West Virginia, USA, in April 1983.~~ Since then, it has received intensive review and editing by specialists in the field and was finally put in a form that is most suitable to occupational health personnel in most countries. The authors of the different chapters represent a reasonable geographic distribution, as was the workshop in West Virginia (list of participants in the Annex). The book also represents one of the many joint activities by WHO and NIOSH in promoting occupational health.

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SUMMARY<sup>1</sup>A. WORK-RELATED DISEASES1. Occupational asthma

Occupational asthma is a reversible obstructive airways disease with hyperresponsiveness of the airways to a variety of allergic stimuli. It is usually associated with symptoms of chest tightness and wheezing together with excessive mucus secretion, mucosal inflammation and edema, and eosinophilia in blood, respiratory tissues and sputum. A diverse variety of vegetable and natural dusts produce occupational asthma, and the global population at potential risk to these dusts is large.

(a) Pathology and pathogenesis. The pathogenesis of occupational asthma is similar to other forms of allergic asthma. Characteristic pathological findings include airway edema and cell shedding, basement membrane thickening, smooth muscle and gland hypertrophy and hyperplasia, and infiltration with eosinophils, associated with overdistension of the lung, but without destructive emphysema. Three major mechanisms are involved in occupational asthma: (1) the induction of bronchial hyperresponsiveness; (2) primary sensitization to an allergen; (3) exposure to nonspecific triggering factors (cold, exercise, viral infection, co-existing chemical irritants).

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<sup>1</sup>By El Batawi, M.A., Finklea, J.F., Glenn, R.E., Major, P.C., Merchant, J.A., Richerson, H.B., Schilling, R.S.F.

Available data suggest that atopy is important in asthma arising from exposure to vegetable and other naturally occurring organic dusts. The presence of IgE antibodies to inhaled antigens defines the atopic individual and plays an important role in triggering asthma in atopic workers exposed to vegetable and other organic dusts. Activation of mast cells leads to release of a large number of mediators which produce bronchospasm, mucosal edema and mucous secretion.

Leukotrienes are now considered leading candidates as primary mediators of asthma, while platelet activation and neutrophil chemotactic activity seem to play a role in the pathogenesis of the disease and should therefore be studied. Cigarette smoking is an important risk factor in airways disease and plays an important role in airways responsiveness.

(b) Clinical assessment. Clinical asthma is a relatively common disease. It has been estimated that 3-5% of the adult population have asthma and that about one-third of those affected will produce specific IgE antibodies to common allergens in their environment. Clinical evaluation depends on assessment of medical and occupational histories, which should include information about specific environmental exposures. Skin testing with specific antigens and radio-allergo-sorbent-test (RAST) may provide useful information about specific antibodies. Clinical assessment can also be aided by documentation of variations in simple measures of lung function (peak expiratory flow (PEF) or forced expiratory volume in one second ( $FEV_1$ ), over a working shift, and if possible, assessment and quantitation of the environmental exposure).

(c) Epidemiology, natural history and management. Available epidemiological data on occupational asthma are limited. There is, however, some evidence that suggests the attack rate of occupational asthma arising from these dusts is dependent on the concentration of dust exposure and the proportion of atopic workers. There are also data indicating that the longer exposure ~~continues following the onset of asthma, the more severe and persistent the~~ asthma symptoms will be. Hence, an important aspect of the medical management of occupational asthma is transfer of affected workers away from exposures. When they cannot be transferred, medical management may require pharmaceutical treatment and the use of respirators, in addition to primary environmental control.

## 2. Hypersensitivity pneumonitis.

Hypersensitivity pneumonitis, also known as extrinsic allergic alveolitis, is a disease with a respiratory and a constitutional component. The disease may occur following the inhalation of antigens contained in a wide variety of organic materials. Offending agents may be bacterial (e.g., thermophilic actinomycetes), fungal (e.g., Alternaria or Aspergillus), serum proteins (e.g., avian or rodent), organic chemicals of defined structure (e.g., toluene diisocyanate), or as yet undefined agents in vegetable dusts (e.g., green coffee dust, insect products).

(a) Pathology and pathogenesis. Much remains to be learned about the pathology and pathogenesis of hypersensitivity pneumonitis. Lung findings in the acute form of the disease are those of an acute granulomatous interstitial pneumonitis with numerous macrophages, giant cells and a modest number of eosinophils. Following repeated insults and persistent chronic inflammation, diffuse interstitial fibrosis or honeycomb lung may develop. Chronic inflammatory changes may persist and the small muscular arteries and

The immunologic events responsible for hypersensitivity pneumonitis are complex. The relevant antigens must reach the appropriate effector cells of the lung. Complement activation may play a role by releasing mediators or interacting with circulating antibodies to form immune complexes. Recent evidence suggests a role for cell-mediated immune responses and for functional abnormalities of T cells.

(b) Clinical assessment. At the time of diagnosis, patients are usually distinguished as having an acute, subacute or chronic form of the disease based upon the clinical presentation. The acute form of the disease is characterized by chills, fever, cough, malaise, inspiratory rales and breathlessness without wheezing, occurring 4 to 12 hours after exposure to the offending environment or antigen. Leukocytosis, restrictive pulmonary dysfunction and hypoxemia are usually demonstrable. The subacute form of the disease has a more insidious onset and is less frequent. This form resembles progressive bronchitis with productive cough, dyspnea, easy fatigue and weight loss. Restrictive and obstructive dysfunction and hypoxemia especially with exercise, may be demonstrable. The chronic form of the disease, resulting from long-term repeated exposures to offending antigens, leads to the gradual development of disabling respiratory symptoms often with pulmonary fibrosis, progressive restrictive dysfunction, reduced lung compliance and hypoxemia.

(c) Epidemiology, natural history and management. Because hypersensitivity pneumonitis is not usually recognized as a reportable occupational respiratory disease, and because patients may be diagnosed as having another respiratory disorder, epidemiologic data are limited. However, the information available suggests that hypersensitivity pneumonitis is a significant, frequently

overlooked illness among farmers and that 3% or more of dairy farmers may be affected. The disorder appears to be more frequent (6-15%) among pigeon breeders. Its frequency among other occupational groups is not known.

~~Education of employees and employers is a logical first step which is necessary for recognition of the disease. It should then be possible for multidisciplinary teams of investigators to identify the offending agents and to develop and evaluate control measure.~~

### 3. Byssinosis

A commonly known occupational respiratory disease resulting from exposure to cotton dusts in ginning, spinning; flax dust in bating and spinning; soft hemp and sisal processing. The disease has been widely investigated in many parts of the world for a large number of years. Byssinosis is characterized by chest tightness and cough which, in the initial stages, appear among the workers in the first day of the working week and/or upon return from holidays in exposure to airborne dusts. As exposure continues the disease becomes a chronic obstructive pulmonary syndrome. Even in its late stages of chronic bronchitis and emphysema, the characteristic symptoms of pulmonary tightness in the first day of the working week still persist. In many instances, particularly with cotton, when cotton is handpicked and processed without storage, these symptoms do not appear, and instead, the workers suffer from upper respiratory tract and eye irritation. After prolonged exposure the worker suffers from chronic obstructive pulmonary disease and emphysema. In all cases of exposure to retted flax, however, the characteristic symptoms of byssinosis are common regardless of the stage of permanent pulmonary impairment.

(a) Pathology and Pathogenesis. The pathological picture of byssinosis is similar to that of chronic bronchitis and in advanced stages to emphysema. A large number of studies have been conducted on the pathogenesis of byssinosis. The main theories are summarized below:

- (i) Histamine release. Several studies show that cotton dust extract, as well as extracts of flax and hemp dusts, induce the release of histamine from samples of human lung tissue in vitro. That the histamine-releasing activity, which is also significant during in vivo exposure of humans, is suggested by the finding that blood histamine levels are higher than normal in flax and cotton workers with symptoms of byssinosis.

Several authors have observed smooth-muscle contraction in guinea-pig ileum in the presence of textile dusts. This may correlate with the prevalence of byssinosis in the mills from which the dust samples were obtained, but similar activity has also been reported with jute dust, which does not cause byssinosis.

- (ii) Gram-negative bacteria and their associated endotoxins. The pharmacodynamics of endotoxins (or lipopolysaccharides) that are found in the cell wall of Gram-negative bacteria have been widely investigated.

In animal experiments, exposure to endotoxins by inhalation causes an influx of leukocytes into the bronchi and the airways. The leukocyte levels remain elevated during a continuous exposure but falls rapidly on cessation of exposure to increase again when the exposure is resumed.

Endotoxins in cotton mill dust have also been measured. The usual concentrations range from  $0.2 \mu\text{g}/\text{m}^3$  to  $1.5 \mu\text{g}/\text{m}^3$  of dust. A good correlation between the extent of byssinosis and the concentration of Gram-negative bacteria in the air has been found in studies in England, the United States of America and Sweden.

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The fact that clear symptoms are more common with stored cotton and retted flax may substantiate this theory from the epidemiological standpoint.

(b) Clinical assessment. Respiratory function studies among the workers exposed show lowering of ventilatory capacity during the day of exposure, sometimes by 15% of the forced expiratory volume in one second ( $\text{FEV}_1$ ) measured before and after the workshift. When chronic obstructive manifestations start to appear, the ventilatory capacity is reduced permanently depending on the degree of respiratory disability. The acute reduction of  $\text{FEV}_1$  during the day also occurs in the advanced cases.

On clinical examination there are no characteristic changes among the workers giving the symptoms. Similarly, the radiographic picture is normal in the early stages. In the advanced stages, changes similar to chronic bronchitis, and later-on-emphysema, appear in chest radiographs.

Recent classification of clinical manifestations  
in respiratory disorders from exposure to vegetable dusts  
causing byssinosis or respiratory tract irritation

Classification	Symptoms
Grade 0	No symptoms
<b>Byssinosis</b>	
Grade B1	Chest tightness and/or shortness of breath on most first days back at work
Grade B2	Chest tightness and/or shortness of breath on the first and other days of the working week
<b>Respiratory Tract Irritation (RTI)</b>	
Grade RTI 1	Cough associated with dust exposure
Grade RTI 2	Persistent phlegm (i.e., on most days during 3 months of the year) initiated or exacerbated by dust exposure
Grade RTI 3	Persistent phlegm initiated or made worse by dust exposure either with exacerbations of chest illness or persisting for 2 years or more

(c) Epidemiology. Byssinosis has been described in many countries producing and/or processing cotton, flax and soft hemp. The disease was first observed more than 120 years ago. It still affects large numbers of exposed workers in many parts of the world. Recent observations of prevalence shows that its magnitude is high, particularly in developing countries, at times affecting up to 60% of the workers exposed.

#### 4. Chronic obstructive pulmonary disease

Chronic obstructive pulmonary disease (COPD) can be caused or exacerbated by exposures to vegetable and other natural dusts. Vegetable dusts contain a mixture of heterogeneous materials. Thus, response to them is mixed and

variable. On present evidence, the main response is non-specific airways obstruction which may lead to chronic obstructive pulmonary disease. However, some exposed workers develop allergic asthma; others may develop hypersensitivity pneumonitis, for example from exposure to moldy rice dust. The chronic obstructive pulmonary disease resulting from such exposures is characterized by increased cough and sputum production which may be associated with airways obstruction.

Pathogenesis. The pathogenesis of nonspecific airways obstruction has not been well defined. There are numerous parallels with airways disease caused by cigarette smoke, the best defined of which is pulmonary disease in grain workers. The effects on the airways include inflammation, increased mucus secretion, increased airways permeability and nonspecific hyperreactivity which can lead to both acute and chronic respiratory symptoms.

The mechanisms by which inflammatory cells are attracted to the lung by vegetable dusts are not understood. Vegetable dusts and other inhaled dusts may contain endotoxins which are known to attract neutrophils, probably by activating the complement cascade that generates chemotactic factors for these cells. These inhaled particulates may also stimulate macrophages, which are present in the airways, to release a chemotactic factor which attracts neutrophils. Once neutrophils are present in the airways, they may release a variety of products which increase mucous secretion, airways permeability, and nonspecific hyperreactivity. The dusts themselves may also stimulate sputum production and histamine release that are likely to increase airways obstruction.

Occupational exposures to dusts causing COPD

1. Grain dusts. The seeding, harvesting, cleaning, transporting, storing and processing of cereal grains can expose workmen to a heterogeneous mixture of substances including husks and particles of grain components, similar particles from weed and other seed contaminants, fungal spores, bacteria, aflatoxins, insect and mite components, and silica, as well as chemical pesticides and herbicide residues.

Workers exposed to cereal grain dusts may develop chronic, progressive airways obstruction. Emphysema has been described in such workers who are nonsmokers or light smokers. Cigarette smoking in addition to dust exposure has an additive or even synergistic effect. Symptoms of cough, sputum, wheezing and shortness of breath are present. Asthmatics commonly select themselves out of the grain industry. Grain workers show evidence of increased airways sensitivity to inhaled histamine and those with alpha-1-antitrypsin phenotype variants appear to be at increased risk.

2. Jute and hard hems. The processing of jute fibers obtained from the stem of the plant, releases dust which in some populations has caused a high prevalence of persistent cough and phlegm, without symptoms of byssinosis. Jute workers have an acute decrement of FEV<sub>1</sub> and forced vital capacity (FVC), during the shift but no studies have yet reported permanent respiratory impairment.

Workers exposed to a mixture of jute and kenaf, a fiber from an East Indian Hibiscus similar to jute, had a high prevalence of chronic bronchitis and a typical chest tightness which, in contrast to byssinosis, worsened

during the week. Respiratory symptoms were related to length of exposure. These workers had reductions in FEV<sub>1</sub> during the shift which were significant in smokers.

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Hard hems are obtained from plant leaves. Studies of workers exposed to Manila, Mauritius and St. Helena hems have similar responses in terms of chest symptoms and acute changes in lung function to those of jute and kenaf, but generally they are less marked.

Present evidence indicates that these dusts cause airways obstruction but not byssinosis. There is no reliable data yet available on exposure/response relations and on evidence of permanent respiratory impairment. There have been no studies of immunology except for dust mixtures which contain jute.

3. Kapok. Kapok is the fiber obtained from the fruits of Ceiba pentandra. Kapok ginners are exposed to excessive dust. In a study of these workers, 78% suffered from mill fever on initial exposure, and 17% of them developed chronic bronchitis which occurred usually after ten years of exposure. It was not related to smoking. Though kapok is similar to cotton, byssinosis was not detected.

4. Coir. Processing of coir, which is the fiber obtained from the husk of the coconut, is dusty. The chief constituents of the dust are lignin (xylogen) and cellulose.

5. Tea. Asthma has been described among workers in tea factories. In one study of 125 tea blenders with an average of 22.9 years in the industry, 36% had respiratory symptoms; 25% had chronic bronchitis and 6% asthma.

6. Coffee. Workers who process, handle and roast green coffee beans are exposed to coffee dust and chaff. In a study of 400 workers, nearly 10% had allergic symptoms consisting of nasal congestion, dermatitis, asthma and lacrymation. Symptoms were attributed to an allergen in raw coffee.

7. Chili. Chili, which is the fruit of shrubs of the genus Capsicum, contains an active principle, capsaicin, which is highly irritant. Workers who grind chilis are exposed to a fine dust. The majority of them develop cough, runny nose and sneezing upon starting work. They develop a relative tolerance after a variable period of exposure lasting up to six months. Workers also experience a burning sensation of the skin and lose weight. Hypersensitivity pneumonitis, as described in paprika splitters, has not been observed.

8. Cocoa. The cocoa fruit contains several seeds, each covered by a mucilagenous coat. After extraction of seeds, this coat is removed by fermentation. In one study, 17 longshoremen unloading cocoa beans in the hold of a ship suffered from nausea, eye irritation, substernal pain, shortness of breath and labored breathing. These symptoms were probably the result of exposure to low oxygen, high carbon dioxide levels, and ethyl alcohol and acetic acid, which are produced by fermentation. Cocoa seeds develop a number of saprophytic fungi which affect the workers in producing countries by symptoms of bronchoconstriction and at times hypersensitivity pneumonitis rather than chronic bronchitis.

9. Cinnamon. Cinnamon, which is obtained from the dry inner bark of Cinnamon zeylanicum, contains an irritant: cinnamic aldehyde. Workers processing cinnamon are exposed to much cinnamon dust and have a high

prevalence of respiratory symptoms (88%) and of asthma (23%). Other manifestations are irritation of skin (50%), hair loss (38%) and smarting of the eyes while at work (23%). Loss of weight (65%) is a common finding.

10. Tobacco. Information on the effects of tobacco dust on the respiratory system is limited. A significant proportion of the world's tobacco products is manufactured in small, often poorly mechanized factories in which dust levels may be very high. Detailed analyses of tobacco dust have not been done. The available data implicate tobacco dust as a cause of chronic bronchitis and possibly occupational asthma. On acute exposure, fever may also be encountered.

11. Rice. Exposure to rice dust may occur during the harvesting, threshing, milling, storage, handling or transportation. The composition of rice dust is not known. Although the amount of epidemiologic data is limited, there are indications that exposure to high levels of rice dust increases the risk of chronic bronchitis and may pose a risk of hypersensitivity pneumonitis.

#### B. METHODS OF INVESTIGATION

Standardized methodology is essential if information from studies by different investigators is to be effectively used. Laboratory procedures are helpful in defining and quantifying health effects of environmental exposures, as well as providing insight into mechanisms of disease. Surveillance programmes may detect patterns of respiratory morbidity or mortality suggesting the need for more detailed investigations. Environmental or biological monitoring may also indicate groups at high risk.

## 1. Respiratory questionnaire appraisal

Standardized questionnaires provide an economical, but partial means of assessing respiratory symptoms and relative levels of exposure to environmental agents. They are a necessary part of any systematic investigation of environmentally related respiratory disease and can also provide information on confounding or modifying factors such as cigarette smoking. Validated questionnaires for byssinosis and chronic respiratory disease have been developed by the British Medical Research Council (MRC). Questionnaires more suitable for investigating the effects of vegetable dust exposures have been developed for cotton workers and grain workers, but at present, these are not validated for occupational asthma and hypersensitivity pneumonitis.

Appropriately modified versions of the MRC versions may be used until validated questionnaires are available. They should retain as much of the content of the original as possible to allow comparison of results with previous studies.

## 2. Pulmonary function appraisal

Standardized spirometric measurement of the forced vital capacity and forced expiratory volume in one second provides the mainstay for functional assessment of the respiratory system. Comparison of results in the study group with appropriate predicted values and if possible with those of a comparable nonexposed control group is essential to interpretation. Measurements made before and after the workshift may detect acute effects of

exposure. Longitudinal studies may provide strong evidence for chronic effects of exposure, but are difficult to carry out effectively.

### 3. Clinical and research laboratory appraisal

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Laboratory procedures which provide information on cellular and humoral responses to exposure may be helpful in several ways. Subclinical effects may be early indicators of disease or may suggest basic pathophysiologic mechanisms. Immune and nonimmune mediated responses may be detected by sampling of serum or bronchoalveolar lavage. Many of the techniques described have limited application in epidemiologic studies and should be confined to carefully designed research studies. Measurement of peripheral leukocyte numbers and differential counts of leukocytes are recommended in studies of vegetable-induced lung diseases and exposures as is the detection of antigen-specific antibody by the double diffusion gel technique. Chest radiographs are helpful in clinical investigations of conditions where intensive transient or chronic parenchymal inflammation or fibrosis occurs (e.g., hypersensitivity pneumonitis), but may be of no use in conditions with very low grade inflammation or predominant airways responses (e.g., occupational asthma). Standardized methods of interpretation are essential to minimize interobserver variation.

### 4. Worker exposure appraisal

Environmental assessment is essential for estimating exposure levels to vegetable dusts which, coupled to duration of exposure, may be related to health effects. This assessment is also useful in determining the efficacy of

existing or newly installed control methods. Individual exposure is best determined with personal samplers, but area samples combined with a detailed job description and time and motion studies will also provide an estimate of personal exposure. Individual cumulative exposure estimates may be derived from work histories combined with historical environmental data, or by assuming that past exposures were similar to present day exposures.

If the primary interest is assessing and controlling exposures, simple methods such as total or respirable personal dust sampling are recommended. If the intent is to relate both exposure and disease with a goal of establishing a safe level of exposure or describing the etiology of the disease, more sophisticated methods may be required: particle sizing, analysis for protein and carbohydrate fractions, endotoxin analysis, and biological sampling for bacteria and fungi. Possible interactive effects due to multiple exposures should be considered, especially where particulates and irritant gases are both present.

The active constituents of vegetable dust are often unknown and may reside in a certain size range of the aerosol. The determination of the active constituents often requires chemical analyses as vegetable dusts are typically composed of a mixture of plant fragments, soil, microbial contaminants, pesticide residues, insect parts, inorganic matter, and animal or insect feces. In general, relating exposure to effect is more difficult with vegetable dusts than with mineral dusts.

## 5. Sampling appraisal

The choice of the sampling method is determined by the physical and chemical characteristics of the dust; the expected concentration; the site of respiratory tract deposition; and the purpose for collection (exposure assessment, particle size analysis, chemical analysis, biological analysis). Different devices are used to collect the total, respirable, or inhalable fractions of any aerosol.

Gravimetric methods are generally used to assess workers' exposure to total dust, respirable dust, and "inhalable" dust. Total dust is typically collected using a 37 mm nonhygroscopic polymeric filter (PVC, etc.) mounted in a plastic cassette and connected to a personal sampling pump, calibrated at 1.5-4 Lpm. Respirable dust may be sampled similarly with the addition of a 10 mm cyclone preceding the filter to remove the nonrespirable particles from the airstream prior to collection. Gram quantities of a total or respirable dust may be obtained by using a high-volume sampler or with a large capacity cyclone preceding a filter. Inhalable dust is monitored using a vertical elutriator designed to collect particles less than 15  $\mu\text{m}$  in aerodynamic diameter.

Inertial impaction particle sizing methods can be employed using either multi-orifice or single orifice cascade impactors. Models are available that require either an external power source or a battery-powered vacuum pump. Vegetable dusts typically contain large particles (lint, etc.) that can clog the impactor orifices or cause excess particle bounce and re-entrainment. Preseparators are available that are designed to minimize these effects.

## 6. Analytical appraisal

Chemical analysis of collected vegetable dust should include analysis for the protein and carbohydrate fraction. Dust can be collected for analysis using total dust or high-volume sampling techniques. Settled dust can be collected with a high-efficiency industrial vacuum cleaner. Analysis for pesticide or herbicide residues should be considered if they are being used on or near the crop concerned.

Biological assessment of vegetable dust may be advisable, especially where vegetable matter is stored for extended periods and when dampness, humidity, and heat encourage the growth of microorganisms. Recommended collection methods include the use of the six-stage microbial impactor, the slit-to-agar sampler, and the all-glass impinger. The first two methods involve direct impaction upon agar-filled Petri plates. Liquid impingement requires the extra steps of serial dilution and plating onto agar surfaces. Fungal or bacterial enumeration can be accomplished using selective media. Measurements are usually expressed in colony-forming units per cubic meter (CFU/m<sup>3</sup>). Identification of the fungi and bacteria is generally advised.

Endotoxin analysis, an assessment of airborne Gram-negative bacterial contamination, should be performed on vegetable dusts. Dust may be collected by area, personal, or high volume samplers, with the appropriate air and volume data to provide quantification of the airborne concentration of endotoxins.

C. PREVENTION AND CONTROL

Occupational respiratory disease caused by vegetable and other natural dusts presents a series of complex problems that hamper efforts directed towards prevention and control. The dusts themselves are poorly characterized. Seasonal variations in crop production and the migratory nature of substantial numbers of the workforce complicate prevention and control. Employees may work long hours for a few weeks, sometimes sustaining relatively high exposures for short periods of time. For such reasons, permissible exposure levels based on an 8-hour workday, 40-hour workweek may not, in some instances, be appropriate. Job assignments involving the greatest risks are not all enumerated, nor are exposed worker populations at increased risk systematically identified. Epidemiologic and clinical studies are generally not available to establish exposure-response relationships. Nevertheless, control principles and measures that are of proven value can help protect the health of workers at risk.

A first step is the identification of health risks which is facilitated by appropriate educational programmes for health professionals, workers and employers. Monitoring exposures in the work environment is a means of identifying potential risks before adverse effects have occurred. Improved reporting systems for occupational respiratory diseases are needed to supplement hazard recognition based upon clinical recognition of new cases of disease.

1. Engineering controls and personal protective equipment

Engineering and environmental controls include enclosure, wetting, local exhaust, and dilution ventilation. When modern technology replaces traditional production methods in developing countries, care should be taken to ensure that appropriate engineering and environmental controls are an integral part of this new technology. Total enclosure and segregation of particularly dusty operations may often be possible. Control of microbial growth may sometimes be achieved. Local exhaust ventilation and sometimes dilution ventilation may reduce high dust levels in workplaces.

Substitution of one fiber or food crop for another may help reduce hazards, but care should be taken to ensure that the new process does not itself present a major health hazard and that the effects on producers and the national economies of developing nations are not unreasonably disruptive.

The use of personal protective equipment may have an important place in reducing exposures where environmental and engineering controls are not possible or practicable. Air purifying respirators may be used for many situations, but supplied air breathing apparatuses may be necessary for certain operations.

2. Medical programs

Health surveillance programs are important in the control of respiratory disorders caused by vegetable and other natural dusts. The effectiveness of health surveillance programs depends upon the willingness of exposed workers

to cooperate. Where preplacement or periodic health examination restricts employment opportunities for the worker, employers should make an effort in good faith to provide therapy of ill workers or alternate employment. Preplacement medical examinations should include a detailed medical history and pulmonary function testing (FEV<sub>1</sub> and FVC). Other measures such as chest radiography, diffusion capacity and evaluation of immune status are reserved for specific situations. In general, care should be taken to place persons with chronic chest diseases, and those with pre-existing bronchial hypersensitivity, in jobs that do not involve dusty work or exposure to airborne irritants. Atopic individuals undoubtedly have an increased risk of sensitization to some agents. However, exclusion of atopics from jobs involving exposure to agents causing occupational asthma cannot prevent such asthma, because nonatopic individuals can be specifically sensitized when exposures are heavy and antigens are potent allergens, as may be the case in many occupational settings.

Periodic examinations, where feasible and practicable, are of value in evaluating the adequacy of environmental controls and in the early identification of health impairment and of susceptible workers. At a minimum, such examinations should include an interim medical history and spirometry. Measurement of diffusing capacity, chest radiography and biological monitoring may be of value in some situations.

### 3. Cessation of cigarette smoking

Smoking cessation education programs are critically important in the control of occupational respiratory diseases. Health personnel, employers and

workers should all be involved. Educational programs are needed to point out how cigarette smoking interacts with exposures to vegetable and other natural dusts to produce chronic obstructive pulmonary disease.

D. RECOMMENDATIONS

Workshop participants from industrialized and developing countries alike agreed that a substantial segment of their worker populations would benefit from efforts leading to the prevention and control of the occupational respiratory diseases discussed. Efficient prevention and control measures are recommended as are areas of research requiring further investigation, which can be facilitated or carried out by the World Health Organization and its Collaborating Centres.

1. Prevention and control

Environmental controls, mentioned below, are considered the most reliable means of reducing or eliminating occupational respiratory diseases. Where these are not possible, feasible or practicable, administrative controls, work practices, personal protective equipment and medical surveillance become more important:

(a) Particular attention should be paid to the control of organic and other natural dusts when designing equipment used in crop production, processing and transportation.

(b) Personal protective equipment should be developed, tested and certified, paying special attention to exposures involving vegetable and other natural dusts.

(c) Information on the availability and suitability of respiratory protective equipment should be made available together with testing facilities for efficacy of this equipment.

(d) Engineering controls, which have had a beneficial effect in reducing ~~or eliminating occupational respiratory disease, should be described~~ and the impact of their use documented.

(e) Since new technologies create new risks and long standing hazards may not be recognized, national administrations should be encouraged to create systematic record-keeping including analysis of health risks associated with new crops and technologies for the purpose of identifying health hazards amongst groups of workers.

## 2. Areas requiring further investigation

Although much work has been done linking occupational respiratory diseases to excessive exposures to vegetable and other natural dusts, further investigations are urgently necessary to fill the present gaps of knowledge. Special attention should be paid to those studies needed for the establishment of exposure-response relationships and for the development of scientifically sound prevention and control programs.

(a) Pathology and pathogenesis. Basic mechanisms underlying the development of byssinosis, occupational asthma, pulmonary hypersensitivity, and chronic nonspecific airways obstruction should be further investigated with special emphasis on the following:

The distribution and fate of inhaled dust components in the lung should be elucidated with special attention being paid to factors thought to play a role in pathogenesis. Research should document the role of inflammatory cells, especially neutrophils, in mediating increased airways permeability, increased mucus secretion, and nonspecific hyperreactivity in individuals with this disorder or in animal models.

Investigations to definitively characterize the mediators in occupational asthma and the roles of lymphocyte, macrophage and eosinophil populations in the pathogenesis of occupational asthma.

The immunopathogenesis of hypersensitivity pneumonitis requires study with emphasis on defining antigens, evaluating the immune response and clarifying the role of genetic factors.

Fiberoptic bronchoscopy with biopsy and lavage may be justified in some patients to provide information on local pathology and associated abnormalities in acute and chronic asthma, during symptom-free intervals, and in hypersensitivity pneumonitis.

Systematic quantitative morphological studies of large and small airways are required in workers exposed to organic dusts.

(b) Clinical studies. Intensive study of individual cases of workers employing clinical techniques and improved systems for classifying and reporting occupational respiratory diseases are needed. Information, on the points outlined below regarding the clinical features of these diseases is

essential for effective therapy, disease reporting and for prevention and control:

- (i) Clinical profiles are needed for individuals and groups of patients thought to be adversely affected.
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- (ii) There is a need to identify factors which may enhance an individual worker's susceptibility to dust exposures. These may include: genetic factors, social and cultural characteristics, infections, tobacco and marijuana smoking.
  - (iii) The effect of childhood exposure to organic dusts on lung growth and function and the relationship of such exposures to the possible development of occupational asthma and chronic obstructive pulmonary disease require evaluation.
  - (iv) Studies are needed to determine whether airways hyperresponsiveness is innate or acquired in occupational asthmas.
  - (v) Chest radiographs are useful tools in the clinical and epidemiological assessment of hypersensitivity pneumonitis, but there is a need to develop standardized techniques and interpretation methods such as exists for the pneumoconioses.
  - (vi) Research leading to more effective therapy for individuals who develop occupational asthma, chronic nonspecific airways obstruction and hypersensitivity pneumonitis is needed.

(c) Epidemiology. More detailed epidemiology studies are needed of workers exposed to vegetable dusts to determine the type of health effects, prevalence, severity and evidence of both temporary and permanent impairment of respiratory function. Whenever practicable and where responses indicate that workers are being adversely affected by exposures to vegetable and microbial dusts, environmental measurements should be made to determine exposure-response relationships to form the basis of control or recommended limits. Specific attention should be paid to the following areas for investigation:

- (i) Systematic efforts are needed to develop data on the number of workers exposed to vegetable and other natural dusts, on the extent of their exposure and in the relative potency of such dusts.
- (ii) Specific recommendations for preplacement and periodic health examination programs should be developed for the workers exposed to the major classes of vegetable and natural dusts.
- (iii) The acceptability and effectiveness of existing and proposed medical surveillance procedures and programs should be evaluated.
- (iv) There is scope for parallel studies to be undertaken in developed and developing countries of workers exposed to vegetable dusts such as grain, rice, tobacco, and animal confinement facilities.

(d) Environmental Monitoring. Monitoring of the workplace environment for vegetable and other natural dusts is a field where further research is required:

(i) Field testing of the environmental monitoring approach is needed

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~~to evaluate the usefulness of the following measurements:~~

inhalable dust, respirable dust, airborne protein, airborne microorganisms, and total dust.

ii) Dusts need to be analyzed for their various components and particle size distributions in terms of respirable and inhalable elements.

CONTRIBUTIONS BY THE AUTHORS

1. OCCUPATIONAL ASTHMA<sup>1</sup>

For the purposes of this monograph, occupational asthma (OA) is defined as reversible obstructive airways disease with hyperresponsiveness of the airways to a variety of occupational stimuli. It is usually associated with symptoms of chest tightness and wheezing together with excessive mucus secretions, mucosal inflammation and edema, and eosinophils of the peripheral blood, respiratory tissues, and sputum. The degree of reversibility is expected to be essentially complete and precipitating factors may be allergic, nonspecific, or idiopathic (Scadding, 1976; Reed & Townley, 1978; Parkes, 1982). The causes of occupational asthma may be divided into those resulting from exposure to grains, flour and plants, to woods, and enzymes (see Tables 1-3).

1.1 Etiological Agents

Exposure to allergenic vegetable dusts is increased in certain occupations, particularly agriculture, food manufacture, forestry, and the commercial exploitation of microbes for animal feed, e.g., Candida utilis and microbial products, proteolytic enzymes and certain antibiotics.

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Table 1. Causes of Occupational Asthma: Grains, Flour, and Plants

Causative Agent:	Occupation:	References:
Grain	Millers Grain handlers	Duke, 1935; Davies et al., 1976; doPico et al., 1977; <del>Skoulas et al., 1964;</del>
	Grain elevator workers	Ise et al., 1973 Chan-Yeung et al., 1979
Flour	Bakers	Ordman, 1947 Papa et al., 1970 Hendrick et al., 1970 Björkstén et al., 1977 Järvinen et al., 1979
Rye flour		Briatico-Vavgosa & Cardani, 1984
Tamarind seeds ( <u>Tamarindus indica</u> )	Millers	Tuffnell & Dingwall- Fordyce, 1957
Green coffee bean	Bean handlers/roasters	Karr et al., 1978
Coffee bean	Bean handlers	Zuskin et al., 1979 Lehrer et al., 1978
Castor bean	Farmers and gardeners Millers and neighborhood residents	Figley & Elrod, 1928 Charpin & Zafiropoulo 1956 Mendes & Cintra, 1954; Ordman, 1955
Tea fluff	Tea shifters/packers	Uragoda, 1970
Maiko-tuberous roots	Millers	Nakazawa, 1983
Gum acacia	Printer	Bohner, 1941; Sprague, 1942; Fowler, 1952
	Drugs and sweets production workers	Brown & Creper, 1947
Gum tragacanth	Gum production workers	Gelfand, 1943
Strawberry pollen	Strawberry growers	Kobayashi, 1974
Cinnamon	Cinnamon handlers	Uragoda, 1984

Table 2. Causes of Occupational Asthma: Woods

Causative Agent:	Occupation:	References:
Western red cedar ( <u>Thuja plicata</u> )	Wood workers Carpenters Timber millers	Chan-Yeung et al., 1973 Chan-Yeung, 1977 Pickering et al., 1972 Gandevia & Milne, 1970 Evans & Nicholis, 1974
Cedar of Lebanon ( <u>Cedrus libani</u> )	Carpenters	Greenberg, 1972
Iroko	Carpenters	Pickering et al., 1972
Californian redwood, <u>Sequoia sempervirens</u>	Carpenters Woodworkers	Chan-Yeung & Abboud, 1976 DoPico, 1978
Mahogany	Pattern makers	Sosman et al., 1969
Oak	Sawmill workers	Sosman et al., 1969
African zebrawood	Woodworkers	Bush et al., 1978
Cocabolla, <u>Dalbergia retusa</u>	Wood finishers	Eaton, 1973
Kejaat, <u>Pterocarpus</u> <u>angblensis</u>	Wood machinists	Ordman, 1949
Obeche, <u>Triplochiton</u> <u>scleroxylon</u>	Carpenters	Innocenti & Augotzi, 1980
Pine resin/colophony	Electronics production workers	Burge et al., 1978 Fawcett et al., 1976

Table 3. Causes of Occupational Asthma: Enzymes

Causative Agent:	Occupation:	References:
<u>Bacillus subtilis</u>	Detergent production workers	Flindt, 1969 Pepys et al., 1969
	Enzyme production workers	<del>Greenberg et al., 1970</del> Newhouse et al., 1970 Mitchell & Gandevia, 1971 Juniper & Roberts, 1984 Juniper et al., 1977
Trypsin	Process workers for plastic polymers	Zweiman et al., 1967 Colten et al., 1975
Pancreatic extracts	Pharmaceutical workers	Pilat et al., 1967
Papain	Laboratory technicians	Tarlo et al., 1978
	Pharmaceutical workers	Baur et al., 1979
Flaviastase	Pharmacist	Pauwels et al., 1978
Bromelin	Process workers	Galleguillos & Rodriguez, 1978

Asthma (and rhinitis) is commonly caused by inhaled organic dusts, suspended in the atmosphere, both outdoors (pollens and mold) and indoors in homes and offices (the house dust mite D. pteronyssinus and domestic pets such as cats and dogs). The prevalence of specific allergens in the environment varies with geographic location, climate, seasons, and time of day.

Exposures to these dusts pose a significant health hazard in developing countries where a substantial proportion of workers are engaged in agriculture. It is important to note that children are frequently exposed to these dusts in the agricultural setting. Hence, exposures to vegetable and other organic dusts are important occupational hazards in both developed and developing countries and involve a population of potential risk which must be measured in the tens of millions.

## 1.2 Pathology and pathogenesis

The general mechanisms involved in occupational asthma appear to be similar to those involved in bronchial asthma, except for certain unique causative agents and the lack of coexisting atopy in some patients with allergic occupational asthma. Consideration of pathogenesis covers initially, therefore, what is known about bronchial asthma, and subsequently consideration of the special features found in occupational asthma.

Pathological findings in patients dying of asthma have included mucosal edema and shedding, basement membrane thickening, smooth muscle and mucus gland hypertrophy and hyperplasia, and airways infiltration with eosinophils.

Overdistension is present without evidence of any form of destructive emphysema; the general architecture of the lung is maintained (Hayes, 1976). The bronchial lumen contains a distinctive exudate composed of a basophilic mucoid component and an eosinophilic proteinaceous element. Some exudate has been found even in asymptomatic asthmatics killed by trauma. Little ~~pathological material has been available from asthmatics during uncomplicated~~ acute or chronic episodes or during symptom-free intervals. Findings at autopsy may not adequately reflect the primary lesions associated with bronchial asthma per se. Fiberoptic bronchoscopy with biopsy and lavage may be justified in some asthmatics, but no such studies have been reported.

The presence of hyperresponsive airways, whatever the basic cause, is currently considered to be the underlying condition predisposing to the development of clinical bronchial asthma. Such airways' hyperresponsiveness can be demonstrated by exercise, hyperventilation, or cooling of airways, and by bronchial challenge with histamine or methacholine in quantities insufficient to produce obstruction in normal airways. The addition of specific allergens, nonspecific irritants, or infection may then result in clinical asthma in individuals so predisposed.

Discussion of pathogenesis of occupational asthma therefore includes airways' hyperresponsiveness; the atopic state; immunologic mechanisms in allergic asthma; causative factors; and specific etiologic agents.

### Hyperresponsive airways in the lung

Hyperresponsiveness of airway smooth muscle in asthmatics may be due to hyperreactivity (an increased responsiveness to every effective dose of a stimulus), hypersensitivity (a decreased dose needed to obtain each response), or both (Daniel, 1981). Possible mechanisms of airways' hyperresponsiveness include prior airway narrowing, hypertrophy of bronchial smooth muscle, autonomic nervous system imbalance, and epithelial damage. Studies so far best support the notion that bronchial hyperresponsiveness in asthma is due to abnormal autonomic regulation of airway smooth muscle rather than to the muscle's contractile mechanism per se. Of the three autonomic systems (sympathetic, parasympathetic, and nonadrenergic inhibitory) regulating muscles of the airways, only the parasympathetic system seems capable of rapid, reversible changes of the magnitude seen in bronchial asthma. Nonadrenergic inhibition in human airways including trachea and small bronchi has been demonstrated, but no evidence has been presented for a defect in the inhibitory system, nor has its role in the airways been defined (Richardson, 1981).

Most studies of airways' hyperresponsiveness have involved atopic subjects. The importance of acquired hyperresponsiveness is suggested by studies of twins (Falliers et al., 1971) and by studies of occupational asthma in which bronchial hyperresponsiveness was the result of chronic exposure to irritating agents and not a necessary preexisting or predisposing condition to the development of occupational asthma (Lam et al., 1979).

The atopic state

Basic mechanisms involved in the production of bronchial asthma are best understood in extrinsic allergic (IgE-mediated) asthma which occurs in atopic individuals. The state of atopy is usually defined as the readiness to ~~develop IgE-class antibodies to harmless inhalants such as pollens, molds,~~ danders, and dusts, as demonstrated by positive wheal and flare skin tests to common inhalant allergens. But of great interest also are the determinant factors for target organ responsiveness: the nose in hay fever, bronchial airways in asthma, and the skin in atopic dermatitis. Atopic asthma appears to be triggered by inhalation of allergens by individuals with specific IgE antibodies, but only if airways' hyperresponsiveness coexists. Thus, the basic factor is the mechanism of airways reactivity discussed above.

Abnormal autonomic nervous system responsiveness has been found in atopic individuals (Kaliner et al., 1982), which may contribute to the pathogenesis of bronchial asthma. Atopic individuals with or without asthma have beta-adrenergic hyporesponsiveness and cholinergic hyperresponsiveness, but only atopic individuals with asthma have alpha-adrenergic hyperresponsiveness. The same investigators found autoantibodies against beta receptors in subjects with beta-adrenergic hyporesponsiveness, but no convincing correlation with asthma could be made in those tested (Kaliner et al., 1982). Although the presence of an autonomic imbalance in allergic (atopic) individuals seems indisputable, the underlying mechanisms and their role in asthma pathogenesis are uncertain. A provocative theory forming a basis for many experimental studies is Szentivanyi's hypothesis of beta-receptor blockade (Szentivanyi, 1980).

The presence of IgE antibodies to inhalant allergens defines the atopic individual; these antibodies play a primary role in triggering bronchial asthma in susceptible individuals.

Immunologic mechanisms in extrinsic allergic (IgE-mediated) bronchial asthma

Allergens. In general, allergens capable of stimulating IgE-class antibodies and subsequently triggering bronchial asthma in individuals with airways hyperresponsiveness consist of organic materials in common inhalants such as dusts, pollens, mold spores, and animal danders. In occupational asthma, similar materials are often involved as well as more exotic inhalants discussed below.

Unique requirements for antigenic determinants capable of triggering IgE immunogenesis have not yet been defined. Although a N-glycosidic protein-sugar linkage incorporated into allergen structures may serve such a role, there is as yet no common primary structural denominator recognized for allergenic structure (Stanworth, 1973).

Antibodies of the IgE and IgG<sub>4</sub> immunoglobulin classes. The antibodies primarily responsible for mediation of extrinsic bronchial asthma are of the IgE immunoglobulin class. Initially recognized as skin sensitizing antibodies capable of passive transfer by Prausnitz and Küstner in 1921 (and called reagins or reaginic antibodies for many years), antibodies responsible for Type I, acute, immediate, anaphylactic-type hypersensitivity reactions were more recently shown to be a new class of immunoglobulin -- IgE (Ishizaka & Ishizaka, 1978).

Evidence has now been presented for the existence of allergen-specific antibodies of the IgG<sub>4</sub> subclass, which may be associated with late responses to bronchoprovocation (Gwynn et al., 1982). The exact role of this antibody class in clinical asthma awaits definition.

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Mechanisms of type I (anaphylactic) hypersensitivity. The combination of allergen with specific IgE antibody takes place on the surface of mast cells and basophils. The bridging of allergen by two antibody molecules (engaged by their Fc portions onto cell membrane receptors which are activated when bridged), begins a series of responses by the mast cell or basophil leading to the release of mediators responsible for clinical manifestations including bronchial asthma (Kulczycki, 1981).

Significant mediators in man include the leukotrienes and histamine, which may affect target tissues directly or via neurogenic reflex arcs or both. Various mediators are either preformed and stored for future discharge or are synthesized as the response takes place. Mast cells in the lung are located in the bronchial lumen, in the submucosa near vessels and glands, throughout smooth muscle, and within the alveolar septa.

Changes associated with triggering of mast cells by bridged receptors include increased phospholipid methylation in the cell membrane, opening of calcium channels and calcium influx, and activation of a serine esterase which leads to mast cell degranulation and release of mediators (Middleton et al., 1981). Mast cell-derived mediators and their sources include: 1) histamine, eosinophil chemotactic factors of anaphylaxis, and neutrophil chemotactic factors of anaphylaxis which are loosely bound to the granule matrix and

quickly released preformed; 2) kallikrein, bradykinin and products of arachidonate metabolism including prostaglandins and leukotrienes which are newly synthesized by the stimulated cell membrane; 3) heparin, superoxide dismutase, peroxidase, arylsulfatase A, chymotrypsin and chemotactic factors for neutrophils and mononuclear cells which are tightly bound, slowly released granule-associated mediators. Recent studies suggest a heterogeneity of mast cells, with defined differences in responses of peritoneal and mucosa-associated mast cells (Pearce et al., 1982).

In addition to bronchospasm, mediator release leads to mucosal edema and mucus secretion. Leukotrienes are the leading candidates as primary mediators of asthma (Holroyde et al., 1981; Lewis & Austen, 1981).

Of considerable interest are reports of platelet activation (Knauer et al., 1981) and neutrophil chemotactic activity during antigen-induced asthma (Nagy et al., 1982). Plasma platelet factor 4 increased within 10 minutes following antigen challenge; the exact mechanisms and significance of the observation need clarification, and observations were not extended into the time of late phase responses. A circulating neutrophil chemotactic factor, however, was found during both early and late asthmatic responses (Nagy et al., 1982). These findings suggest that mediators of hypersensitivity are released in late as well as early asthmatic responses.

The role of the eosinophil, whether protective or injurious to host tissue in bronchial asthma, has not been precisely defined and demands further study (Butterworth & David, 1981). Evidence has been marshaled to suggest a

modulating role for eosinophils on the allergic response, and more recently an inflammatory role has been suggested for its major basic protein (Frigas et al., 1981).

Late responses in asthma, as in allergic alveolitis, were initially ~~considered manifestations of Type III (immune complex-mediated) reactions but~~ no evidence of this has been forthcoming. What roles, if any, lymphocytes and their products (lymphokines) play in these responses also await definitive exploration. Activation of complement via the alternative pathway has been nonconfirmatory (Monie et al., 1979). Serum levels of these various potential components of the heterogeneous asthmatic response may not adequately reflect changes occurring at local bronchial sites.

Causative factors: early and late responses

The use of bronchoprovocation, and longitudinal studies after known exposures (feasible in occupational asthma), have revealed two components to airway obstruction following challenge: an early (immediate) asthmatic response and a late (nonimmediate) asthmatic response. These observations have enlarged our understanding of clinical asthma and its pathogenesis (Dolovich & Hargreave, 1981).

Early responses occur within minutes and clear, usually spontaneously, within an hour or so of challenge with an antigen; they also result from hyperventilation; exercise; or inhalation of cold air, histamine, and methacholine. The early response is not followed by an increase in nonspecific bronchial responsiveness (i.e. hyperresponsiveness), but is greatly dependent upon the pre-existing state of bronchial hyperresponsiveness of the host.

Evidence suggests that early responses are simply reversible smooth muscle contractions, whether due to mediator release or to irritant-receptor-vagal reflexes.

Late responses, on the other hand, occur 6 to 12 hours after an early response to inhaled antigen in perhaps 50% of allergic asthmatics. These late responses simulate naturally occurring asthma more closely than do early responses in several respects. Late responses last longer, are more resistant to treatment, are associated with greater degrees of obstruction, and are prevented by corticosteroids which have little effect on early responses. Clinical improvement following immunotherapy with house dust mite extract was found to be associated with loss of the late but not of the early response to antigen rechallenge. Late cutaneous reactions to allergen can be attributed to consequences of IgE antibody-mediated responses alone (Richerson et al., 1979). The pathogenesis of late responses appears to involve a major inflammatory component. Late asthmatic responses to antigen are associated with an increase in nonspecific bronchial responsiveness.

Hyperresponsiveness is also acquired following virus infections, inhaled chemically-reactive substances and pollutants such as ozone. Such stimuli appear to induce asthma as an acquired condition, suggesting that asthma may be generally acquired as a result of exposure to inducers. Indeed, this was pointed out by Dolovich and Hargreave in 1981.

In summary, the occupational environment may be responsible for the appearance of bronchial asthma by several different mechanisms: 1) induction of bronchial hyperresponsiveness; 2) primary sensitization to an allergen; and

3) exposure to nonspecific triggering factors. Agents stimulating reversible airways obstruction (inciters) may do so by sensitization as an allergen in atopic or in nonatopic individuals, or by nonallergic mechanisms involving inflammatory, pharmacologic, or neurogenic pathways (Murphy, 1976).

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When vegetable dusts are the causative agents, the most common sequence is presumably induction of airways hyperresponsiveness and allergic sensitization with the subsequent onset of clinical asthma, most often in an atopic individual. Coexistent environmental factors including nonspecific irritants, toxins, chemicals, cold dry air, exercise, viral infections and other intercurrent illnesses during induction or inciting phases may be important and add to the complexity of definitive evaluation. Cigarette smoking is undeniably an important risk factor in the development of airways disease and often overrides all other factors (Weill & Diem, 1980).

### 1.3 Clinical and Epidemiological Review

The typical picture of occupational asthma is easy to recognize. The principal complaint is wheeziness at work. However, wheeziness is often preceded by conjunctivitis, rhinitis and sneezing. Frequently the first manifestation of occupational asthma is a nonproductive cough, which over a period of several months, or even years, develops into wheezing. The predictive symptoms of incipient asthma are clearly related to the working environment; however, wheezing does not necessarily occur during work hours. In a late asthma reaction, the symptoms may start after the workshift, in the evening or even at night. Thus the association between symptoms and the working environment in late reactions may easily be overlooked.

If the symptoms resolve rapidly, the patient may experience the same degree of symptoms over each workshift. If the night is too short for the symptoms to resolve, a progressive deterioration may be felt throughout the week. As a rule, the early symptoms of occupational asthma tend to disappear over weekends and holidays. However, as a consequence of the cumulative effect of repeated exposure, the symptoms may need more than two days to resolve. At this stage the asthma begins to worsen week by week. The longer the workers remain exposed, the greater the risk that they will begin to react to totally unspecific stimuli such as dusts, exhaust fumes, tobacco smoke, cold air, physical exercise, and so on.

The examination of a patient suspected of suffering from occupational asthma involves the same basic battery of tests and investigations as those used in the diagnosis of any asthmatic. The first task is to assess whether the patient is in fact suffering from asthma. (For an excellent example of

the routine investigation, see, for example, Crofton and Douglas, 1981). The second task to be assessed is whether there is a causal relationship between the symptoms and the working environment. The demonstration of specific antibodies is an important part of the diagnosis. Commercial allergen extracts are available for many organic allergens and ad hoc extracts can often be produced. Due to toxic reactions, chemicals are not always suitable for skin testing. Serologic methods, such as the radio-allergo-sorbent-test (RAST), provide a means of demonstrating specific antibodies in the serum. Nasal and conjunctival provocation tests offer valuable alternatives.

A convincing history, together with skin and serologic test results, combined with the demonstration of ventilatory function decline may suffice for the diagnosis. For medicolegal reasons, or if the offending agent is not a known inducer of occupational asthma, it may be necessary to produce more irrefutable evidence of a causal relationship. Such proof can be obtained by inhalation challenge tests (Pepys & Hutchcroft, 1975), which may be performed either under controlled conditions in a hospital or at the workplace.

Records of peak expiratory flow at work may be obtained over a prolonged period (10 days - 4 weeks). Poor recording techniques, unknown levels of exposure, and medical treatment may interfere with the records. The procedure, though rather demanding for the worker, has proven most useful in the diagnosis of occupational asthma; however, it cannot identify the specific agent causing the disease (Burge, 1982a).

To obtain a specific etiological diagnosis, inhalation provocation tests under controlled conditions should be used. Knowing the agent may be of the utmost importance to the patient, who may have to change jobs within the plant

or transfer to a totally different industry (Davies & Pepys, 1977). The provocation techniques available today are simple, safe, and reproducible and can be applied for a variety of industrial dusts, vapors, and fumes. The techniques have been described in detail by Newman Taylor and Davies in 1981. The amounts and concentrations used for exposure should be carefully guided by the history and information on the working conditions. Some agents may induce asthma in sensitized subjects at extremely low levels (e.g., isocyanates) and require simultaneous monitoring of the concentrations in the exposure chamber.

Inhalation provocation tests are time consuming for several reasons. Single challenge tests can be performed only once a day. The next challenge should not be attempted before total recovery. The results are interpreted by comparison of the reaction with both spontaneous variation and the result of a placebo test. It should be emphasized that inhalation challenge tests cannot be performed on patients suffering from unstable asthma. Adequate medical treatment, frequently including oral steroids and the interruption of exposure, may be needed for several weeks before provocation tests can be done.

Test reactions to bronchial provocation. The reaction provoked by an inhalation challenge test may develop within a few minutes of exposure or as a late reaction. Late, that is, nonimmediate, reactions display different patterns, all of which are thus far only descriptive. The mechanisms of these reactions are not well understood. Sometimes a challenge test is followed by a dual response, i.e., both an immediate and a late reaction (Newman Taylor & Davies, 1981).

The immediate reaction, as described by Pepys and Hutchcroft (1975) starts within 10-15 minutes of exposure; reaches its maximum within 15-30 minutes; and resolves within 1 to 2 hours. The immediate reaction is known to be inhibited by sodium cromoglycate. It can also be inhibited by the administration of a  $\beta_2$ -adrenoreceptor stimulant, whereas oral or inhaled ~~corticosteroids taken prior to the test~~ have no inhibitory effect. The asthmatic reaction is reversed by the inhalation of  $\beta_2$ -adrenoreceptor stimulants.

According to Pepys and Hutchcroft (1975), three types of nonimmediate asthmatic reactions can be distinguished. Reactions that start 4-8 hours after exposure and resolve within 24 hours can be inhibited by oral or inhaled corticosteroids taken prior to the test. Sodium cromoglycate taken before the test or during the day of the test may also inhibit the reaction partially or even completely. The effect of  $\beta_2$ -adrenoreceptor stimulants is not as good; they produce a partial and temporary improvement in lung function.

Another type of late reaction starts about one hour or more after exposure and persists for 3-4 hours. Frequently the reaction comes in the early hours of the morning. This type sometimes tends to recur at the same time on a number of successive nights. The recurrent nocturnal reaction may follow one single exposure and has been caused by isocyanates and penicillin dust (Pepys & Hutchcroft, 1975; Newman Taylor & Davies, 1981).

As inhalation challenge tests place great demands on the patients as well as on health personnel, they should be performed in centers where expertise in occupational respiratory diseases is available, and patients should be channeled to such centers (NIAID Task Force Report, 1979; Pepys, 1982).

Epidemiology

Reliable estimates of the risk of developing occupational asthma in workers exposed at work to particular allergens are difficult to obtain, and subject to biases which make valid analyses of the relationship between exposure and risk of disease unreliable. These include:

Case Identification - There is as yet no reliable method of identifying cases of occupational asthma in exposed populations. Different studies use various definitions of case status based on the results of symptom questionnaires, lung function test measurements, and immunologic reactions.

Selective biases - Individuals who develop occupational asthma are likely to avoid further exposure to the cause of their asthma, and leave their place of work.

Exposure disease relationships - The tendency of individuals who develop this disease to avoid further exposure to its cause means that those who accumulate exposure are those who survive to do so.

These problems make it difficult to generalize from prevalence surveys which form the majority of studies of occupational asthma. Some longitudinal studies of occupational asthma have been undertaken. The majority of these are serial prevalence surveys which suffer from the problem of not knowing the reason for leaving among those who cease employment in the industry. Probably the most satisfactory solution to this problem is to study employees exposed

at work to a particular allergen. Such studies would include regular investigation of the exposed population, with symptom questionnaires, lung function test measurements and where appropriate, immunologic investigations, as well as ascertainment of reasons for leaving employment where appropriate.

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Juniper and coworkers (1977), in a prospective seven year study of those employed in a factory manufacturing enzyme detergents, studied 1642 employees with symptoms questionnaires, lung function test measurements and skin prick test reactions, both to common inhalant allergens (as a measurement of atopy) and to Bacillus subtilis enzyme alkalase. The reasons for leaving employment or relocation in the industry, were ascertained. In addition, regular measurements of atmospheric enzyme dust were ascertained. They found that the rate of disease was increased in those most heavily exposed to enzyme dust and among atopics. The rate of disease decreased with improvements in dust control, during the seven year period.

Another study, of chemically induced occupational asthma from toluene diisocyanate workers (TDI), indicated that asthma symptoms may persist for several years and even worsen without any further exposure to isocyanates (Adams et al., 1978). In several workers with colophony asthma, their symptoms persisted after they left the work. Symptoms on follow-up were common, and only 14% of those affected had returned to the state of health they had before developing asthma (Burge, 1982b).

A recent careful follow-up of red cedar workers also indicated a guarded prognosis, even among workers removed from the environment (Chan-Yeung et al., 1982). Early diagnosis and removal from exposure were associated with

recovery, but only about one-half of all workers recovered completely after their exposure ended; the mean period of follow-up was three and a half years. Methacholine challenge demonstrated bronchial hyperresponsiveness at the time of initial diagnosis. This test gradually returned towards normal in patients who became asymptomatic after removal from the environment; in only 8 of 26 of these asymptomatic individuals was the methacholine challenge test within the normal range. Similar observations have been made on platinum salt workers (Newman Taylor, personal communication) and recently have been noted among 88 cases of isocyanate asthma (Nordman, personal communication). These studies therefore suggest that the reduction of bronchial hyperresponsiveness is slow to reverse and may not reverse if exposure to the inducing agent is prolonged.

#### Specific examples of occupational asthma

Grains and flour. Occupational asthma occurs in those exposed to grain dusts during harvesting, transport, storage, and milling and also in those exposed to flour dust in bagging, transportation, and use (see Table 1). Grain dust is a complex mixture of the grain, i.e., wheat, barley, oats, etc., and various contaminants, particularly fungi and mites, many of which are allergenic. The microflora of grain dust differs considerably at harvest time and in storage. The major contaminants of harvest dust are saprophytic field fungi, such as Cladosporium, Alternaria, Verticillium, Paecilomyces and plant pathogens such as Ustilago. Fungal spores and hyphae are the major constituents of airborne harvest dust. In one study, airborne dust around combine harvesters contained up to 200 000 000 fungus spores per cubic millimeter with Cladosporium accounting for more than one-half of the total

spores (Darke et al., 1976). Grain handled between harvesting and storage has a similar flora. Once placed in storage, the change in the microflora depends chiefly on water content, the degree of spontaneous heating, and the aeration of the grain. If the aeration is restricted as in sealed silos, heating and microbial growth is limited unless a leak of air occurs during unloading.

~~Species of yeast and Penicillium are most abundant in these circumstances.~~

With increasing aeration, low water content and temperature, the predominant species is Aspergillus glaucus. As water content increases, these are replaced by other Aspergillus species and at a water content of 30% and temperature between 50°C and 65°C, the predominant species are Aspergillus fumigatus and thermophilic actinomycetes, such as Micropolyspora faeni and Thermoactinomyces vulgaris. Malting may encourage the growth of Aspergillus clavatus. In addition, grain in storage may be contaminated by mites such as Tyrophagus longior and Lepidoglyphus destructor.

Several studies of grain workers have identified the risk of occupational asthma, but in few cases has it been possible to identify with confidence, the specific cause. Darke et al., (1976) studied Lincolnshire farm workers in the United Kingdom. One quarter complained of respiratory symptoms when exposed to harvest dust, a proportion of whom were found to have evidence of specific IgE antibody to the harvest fungi. Chan-Yeung and coworkers (1979) found that 4% of 610 grain elevator workers in British Columbia, Canada, had a decrease in FEV<sub>1</sub> greater than 10% during a working week. They studied 22 of these, six of whom had asthmatic reactions provoked by grain dust challenge, and 16 of whom did not. They obtained no immunologic evidence to identify the specific cause of their asthma in these six. Ingram and colleagues (1979), obtained evidence to suggest that storage mites, Tyrophagus longior and Lepidoglyphus destructor caused asthma in farmers, in the Orkneys, Scotland, exposed to hay and grain dust.

Molds which grow in grain due to storage tend to be associated with extrinsic allergic alveolitis rather than asthma, although Aspergillus clavatus have been shown to cause asthma, as well as allergic alveolitis.

Flour dust is a complex mixture of starch and proteins which is less likely to be contaminated by mold and mite allergens than grain dust, but to which other allergenic materials may be added during food production. Occupational asthma in bakers is well described and is the major cause of occupational asthma in Finland. Immunologic studies have identified specific IgE antibody to wheat and rye flour, proteins in affected bakers.

Castor beans. Allergic reaction from the upper respiratory tract caused by castor bean dust has been recognized since the 1920s. The allergenic fraction in castor bean and its composition have been studied by Coulson and coworkers (1950). Most of the workers sensitized to castor bean have been millers working inside the bean processing plant (see Table 1.). However, sensitization to castor bean was also noted among coffee bag handlers. The cause of their sensitization to castor bean was most likely the fact that the same bags had previously been used to transport castor beans (Figley & Rawling, 1950). Asthma has been shown to develop in farmers and gardeners using a dried residue of the beans as fertilizer. Specific IgE-antibodies have been demonstrated in the sera of patients with clinical symptoms and positive skin prick tests.

An extremely interesting feature of the castor bean is that it has caused endemic outbreaks of asthma in residents living in the vicinity of bean processing plants. The first outbreak occurred in Toledo, Ohio, in the United States of America (Figley & Elrod, 1928). Other similar outbreaks with

asthmatic bouts both inside the factory and among neighboring populations have occurred in Brazil (Mendes & Cintra, 1954), South Africa (Ordman, 1955), France (Charpin & Zafiropoulo, 1956), and the last one in Dieppe, France (Wolfrohm et al., 1967). These incidents are interesting because an industrial pollutant is rarely strong enough to cause sensitization in the ~~neighboring population. Another possibility is that such epidemics have been~~ overlooked.

Pyrethrum. Although primarily an irritant of the skin, pyrethrum plays a significant role in the genesis of asthma associated with its industrial processing. The etiologic agent is derived from the flowering plants, Chrysanthemum pyrethrum and Pyrethrum cinerariaefolium, which grow in various parts of Africa, the Americas, Asia, Australia, and Europe. Large scale commercial plantation occurs principally in Kenya. The powdered pyrethrum is widely used as the active ingredient in agricultural and cattle insecticides (Hunter, 1978; Casida, 1973).

The respiratory effects of exposure to pyrethrum dust may be vary clinically. The dust irritates mucosal linings of the bronchi and bronchioles (ACGIH, 1974; Hunter, 1978). Hay fever-like symptoms, wheezing, and breathing difficulties may occur from exposure (Gleason et al., 1969; Hayes, 1963; Heyndrickx, 1969; NIOSH, 1981).

A few cases of occupational asthma due to pyrethrum mixtures have been reported (NIOSH, 1981). In persons with chronic respiratory disease and especially asthma, the inhalation of pyrethrum may cause exacerbation of symptoms due to its sensitizing properties (NIOSH, 1981). Pyrethrum pollen has been reported in Japan to cause frank occupational asthma (Natagawa & Katsuta, 1974).

Wood dusts. Several wood dusts are known to cause asthma. Most of these are listed in Table 3. In general, hardwoods, such as redwood cedar, are able to cause sensitization. Carpenters, sawmill workers and joiners are at special risk. The most common causes of asthma are western red cedar, iroko, mahogany, cedar of Lebanon, and obeche.

The asthmatic reaction can be both immediate and late; even dual responses have been recorded. Late reactions appear more common (Gandevia & Milne, 1970; Pickering et al., 1972; Chan-Yeung, 1977).

One of the best known types of wood-induced asthma is that caused by the western red cedar (Thuja plicata). Plicatic acid is a low molecular weight compound isolated from western red cedar. In bronchial provocation tests, plicatic acid was subsequently incriminated as the agent responsible for the asthmatic reaction to red cedar (Chan-Yeung et al., 1973). The latency period between exposure to the wood and the development of symptoms appears to be relatively short; asthma usually develops after a few months of exposure. The late reaction that occurs after the workshift makes it difficult to associate the symptoms with the wood dust and may lead to self-selection among the workers in the industry. A follow-up study of 38 patients with red cedar asthma showed that the symptoms may persist for more than six months; however, 27 patients became asymptomatic after they left the environment of exposure (Chan-Yeung, 1977).

Pyrethrum dust occasionally causes sensitization and the affected worker may suffer from an anaphylactic type of reaction. Some persons exhibit sensitivity similar to pollinosis with sneezing, nasal discharge, and nasal

stuffiness (NIOSH, 1981). The dust may also irritate the eyes (Grant, 1974; NIOSH, 1981) causing transient conjunctival edema, hyperemia, and sometimes photosensitivity or facial edema (Hunter, 1978).

A few cases of asthma due to pyrethrum mixtures have been reported. No ~~available data on levels of exposure, dose-response relationships, lung~~ function tests, or other related parameters are found in the literature. Epidemiologic studies should be carried out in countries where pyrethrum powder is used. Studies aimed at defining the composition of the dust and its effects should be undertaken.

Medical management. The management of established cases of occupational asthma is straightforward and the principles of treatment do not differ from those of other forms of asthma. Individuals with established asthma should be removed from exposure. This can be accomplished inside the same factory but this is not always practicable. Transfers inside or outside a plant, may involve socioeconomical obstacles which make the diseased worker unwilling to make such a transfer. In such cases, or when the workers are middle-aged and selectively skilled with little chances for reeducation, they may have to be kept at work under medical supervision and treatment. The most frequently attempted therapy is sodium cromoglycate. This therapy has sometimes proven successful; however, there are no longitudinal studies that assess the prognostic hazards probably involved in cases of continuing exposure. Whenever the exposure of an individual with established occupational asthma continues, long-term medical supervision will be required (Parkes, 1982). There is data that suggests some workers may improve clinically or lose their clinical symptoms completely even with further occupational exposure (Thiel, 1983).

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## 2. HYPERSENSITIVITY PNEUMONITIS<sup>1</sup>

Hypersensitivity pneumonitis comprises a syndrome of allergic lung disease resulting from sensitization and recurrent exposure to any of a variety of inhaled organic dusts. The disease occurs as a diffuse, predominantly mononuclear inflammation of the lung parenchyma, particularly the terminal bronchioles and alveoli. The inflammation frequently organizes into granulomas and may progress to fibrosis in chronic cases. A wide variety of dusts such as moldy fodder in farmer's lung, moldy sugar cane in bagassosis, bird droppings or other avian proteins in bird breeder's lung, and fungal spores in cheese worker's lung can cause the disease. Most individuals who develop hypersensitivity pneumonitis are exposed through their occupation. However, sensitizing organisms have recently been shown to contaminate and be dispersed through forced-air heating, air conditioning or humidification systems, causing pulmonary disease in home and office occupants.

No single clinical feature or laboratory test is diagnostic of the disease. Rather, the diagnosis is made from a combination of characteristic historical symptoms, physical findings, X-ray changes, pulmonary function abnormalities and immunologic tests. The demonstration of precipitating antibodies to a suspected environmental antigen is particularly helpful. Occasionally, lung biopsy or inhalation challenge is of value.

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## 2.1 Etiologic agents

Hypersensitivity pneumonitis may occur following the inhalation and subsequent sensitization of antigens in a wide variety of organic materials. Offending agents may be bacterial (thermophilic actinomycetes), fungal (Alternaria, Aspergillus), serum proteins (avian or rodent proteins), chemical (anhydrides), or yet undefined (coffee dust). A list of such agents is shown in Table 4.

Table 4. Some etiologic agents of hypersensitivity pneumonitis

Agent	Disease	Exposure	Country in which produced
<u>Definite causative</u>			
Thermophilic actinomycetes			
<u>Micropolyspora faeni</u>			
<u>Thermoactinomyces vulgaris</u>	Farmer's lung Mushroom worker's	Moldy compost Moldy mushroom compost	Universal
<u>Thermoactinomyces viridis</u>			
<u>Thermoactinomyces saccharii</u>	Bagassosis	Moldy sugar cane	Universal
<u>Thermoactinomyces candidus</u>	Ventilation pneumonitis	Contaminated forced air system	
Fungi			
<u>Cryptostroma corticale</u>	Maple bark stripper's disease	Moldy maple bark	United States of America
<u>Aspergillus clavatus</u>	Malt worker's lung	Moldy malt	USA United Kingdom
<u>Aspergillus fumigatus</u>	Hypersensitivity pneumonitis	Compost	
<u>Penicillium frequentans</u>	Suberosis	Moldy cork dust	Portugal
<u>Penicillium caseii</u>	Cheese worker's lung	Cheese mold	Switzerland
<u>Alternaria sp.</u>	Wood worker's lung	Moldy wood chips	USA
<u>Pullularia sp.</u>	Sequoiosis	Moldy redwood dust	USA
<u>Mucor stolonifer</u>	Paprika splitter's lung	Paprika dust	Hungary
Arthropods			
<u>Sitophilus granarius</u>	Wheat weevil disease	Infested wheat	USA UK
Animal proteins			
Avian proteins	Bird breeder's lung	Avian droppings	Universal
Rat urinary proteins	Laboratory handler's lung	Urine protein	USA UK
Chemicals			
Phthalic anhydride	Epoxy resin worker's lung	Epoxy resin	USA
Toluene diisocyanate	Porcelain refinisher's lung	Paint catalyst	USA
Trimellitic anhydride	TMA disease	Trimellitic anhydride	USA

Table 4. (continued)

Agent	Disease	Exposure	Country in which produced
<u>Probable causative agents</u>			
Ameba, various fungi	Ventilation pneumonitis	Contaminated systems	Universal
<del>Bacillus subtilis</del>	<del>Enzyme worker's lung</del>	<del>Detergent powder</del>	<del>USA UK</del>
Hair dust	Furrier's lung	Animal proteins	Universal
Coffee dust	Coffee worker's lung	Coffee beans	USA
Altered humidifier water	Humidifier lung	Humidifier water	Universal
Various saprophytic fungi	Hypersensitivity pneumonitis	Contaminated environments	Universal

The major occupations and industries associated with hypersensitivity pneumonitis are those in which there is exposure to moldy vegetable compost, that by its very nature is contaminated with thermophilic actinomycetes. The dust of compost contains spores of organisms which are less than 1  $\mu$ m in size and can thus travel and lodge in the terminal airways and alveoli where they can react. Thus, farmers (Campbell, 1932; Dickie & Rankin, 1958), sugar cane workers (Lacey, 1976), compost handlers (Vinckem & Roels, 1984), and mushroom compost handlers (Bringhurst et al., 1959) are exposed, as are individuals living or working in environments with ventilation systems contaminated with these organisms (Banaszak et al., 1965; Fink et al., 1971).

Employees in industries, in which dust from wood products can be inhaled, are prone to the development of hypersensitivity pneumonitis. Suberosis (cork) (Avila & Villar, 1968), sequoiosis (redwood) (Cohen et al., 1967), maple bark stripper's disease (Emanuel et al., 1966; Towey et al., 1932), and wood pulp worker's disease (Schlueter et al., 1972) are found in such industries. Individuals involved in bird handling (pigeon racers, pigeon showers, budgerigar raisers) develop disease as a result of the inhalation of proteins from droppings, dander, saliva and urine (Faux et al., 1971; Fink et al., 1972; Pepys 1969; Reed et al., 1965).

The disease had also been described in plastic fabricating industries, especially when isocyanates and anhydrides are used (Fink & Schlueter, 1978; Schlueter et al., 1978). Such areas include epoxy or urethane paint spraying and epoxy manufacture.

More recently, it has been recognized that environments with ventilation systems of forced-air heating, cooling or humidification may become contaminated with a wide variety of microorganisms. Persons living or working in such environments are susceptible to the development of hypersensitivity pneumonitis as a result of repeated inhalation of those contaminants (Banaszak et al., 1970; Edwards et al., 1976; Fink et al., 1971; Fink et al., 1976; Friend et al., 1977; Hodges et al., 1974; Miller et al., 1976; Tourville et al., 1972).

Other industries in which hypersensitivity pneumonitis may occur are variable and have little in common. As new areas of exposure and subsequent diseases are described, it has become apparent that a broad variety of inhalant organic dusts is capable of inducing hypersensitivity pneumonitis.

## 2.2 Pathology and Pathogenesis

The lung is an unequalled organ in that it receives during the respiratory processes an extremely large number and variety of potential antigens. Important antigenic agents present in organic dusts are derived from fungal, bacterial, serum protein, or chemical sources. Due to the small particle size of these dusts (usually less than 5  $\mu\text{m}$ ), large quantities of antigenic material can be deposited at the alveolar level as well as in the airways. Under certain circumstances, this antigen load results in an immunologic response producing reactions in the airways and lung parenchyma. The clinical response to this challenge depends on the individual's immunologic reactivity, i.e., atopic or nonatopic, the nature of the dust, the size of the particles, and the intensity of exposure, particularly whether it is regular or intermittent (Pepys 1969).

The pathologic abnormalities depend on the timing of the antigen exposure, the character of the offending antigen, and the host response. In different clinical entities such as farmer's lung, bird fancier's lung, mushroom worker's lung, etc., the pathologic events occurring in hypersensitivity pneumonitis are similar during the course of the disease. The intensity of any acute inflammatory events appears to vary with the antigen dose delivered to the lung and the interval between acute exposure and past episodes.

The lung morphology during acute clinical episodes is that of an acute granulomatous interstitial pneumonitis. The alveolar spaces contain numerous macrophages and foreign body giant cells, as well as neutrophils and a modest number of eosinophils. The macrophages frequently contain stainable neutral fat. The alveolar walls are thickened, edematous, and infiltrated by neutrophils, a few eosinophils, and macrophages. As the chronicity of the process develops, the inflammatory exudate within the interstitial tissue has more of a plasmacytic or lymphocytic character. The inflammatory exudate is paucicellular in the earliest stages; some fibrinous exudate may also precede the inflammatory exudate. The granulomatous lesions consist of dense collections of plump epithelioid cells arranged in palisaded fashion, frequently surrounding zones of liquefaction necrosis in which some necrotic tissue debris and a few inflammatory cells remain. Bronchioles are often involved and demonstrate a necrotizing process which destroys portions of their mural structure and occludes the bronchiolar lumen with macrophages, inflammatory cells, and tissue debris. The bronchiolar epithelium may be destroyed and replaced by a flat, regenerating epithelium. The involved adjacent alveoli are lined by hypertrophied, cuboidal epithelial cells (Barrowcliff & Arblaster, 1968; Reyes et al., 1982).

As the process unfolds, its course may be influenced by several factors: the degree of sensitization to the offending specific antigenic material, the amount of antigen available in the current episode, and the number and timing of any repeat exposure to the same antigen. If the degree of sensitivity is minimal or the antigen dose encountered during the inciting episode is small ~~with the encounter not repeated, the inflammatory episode may resolve with~~ little or no residual tissue change. If the inflammatory process persists, either due to persistence of the chronic reaction or the periodic recurrence of acute exacerbations, the lung will incur insidious or episodically overt continued tissue destruction. Noncaseating granulomas may then be seen with greater frequency. The inflammatory exudate within the alveolar spaces and bronchial lumina may become invaded with fibroblastic cells and will contain distinctive collections of fibrous tissue known as Masson bodies, which are evidence of the organization of alveolar exudate. The chronic inflammatory exudate within the interstitial and alveolar septa increases in amount; becomes characterized by a greater number of plasma cells; and thickened by fibroblastic invasion and hypertrophied alveolar epithelial cells (Reyes et al., 1982).

Following a prolonged period of repeated acute insults and persistent chronic inflammation, diffuse interstitial fibrosis or honeycomb lung may develop. Within the fibrosis, inflammation may persist in the interstitial and alveolar septa which have become thickened by mature collagenous connective tissue and some residual chronic inflammatory cells. Noncaseating granulomas are infrequent or absent and may be replaced by collagen or hyalinized tissue. The alveolar spaces are modestly enlarged and the walls thickened by fibrosis and alveolar cell hyperplasia. Intra-alveolar organizing Masson bodies are seen. Small muscular arteries are thickened and sclerotic.

In honeycomb lung, a similar residual chronic inflammatory process may be present in the interstitial and intra-alveolar spaces and the airspaces are enlarged and cyst-like, reaching a dimension of 0.5-1.0 cm. The walls of these spaces are fibrotic, contain elements of hypertrophied smooth muscle, plasmocytes and lymphocytes, and are frequently lined by hypertrophied bronchial epithelial cells. The muscular arteries and arterioles are markedly thickened.

The characteristic abnormality in acute tissue reaction is acute inflammation along with granulomas composed of plump epithelioid cells with necrosis and tissue destruction. The presence of large foamy macrophages has been most frequently observed in bird fancier's lung (Hensley et al., 1969).

When the number and varieties of substances inhaled as a result of environmental exposure are considered, the potential antigens for hypersensitivity pneumonitis are almost infinite. A complex relationship must exist between the type and dose of the inhaled antigen, the removal mechanisms, and the defense system of lungs. Further, in order for disease to be induced, relevant antigens must contact the immune effector cells of the lung. There is some recent evidence that specific antigens, which induce a specific immune response, may be required for induction of disease (Calvanico, N.: Personal communication).

The presence of serum precipitins to the inhaled antigen is the immunologic hallmark of hypersensitivity pneumonitis (Pepys 1969). Precipitins are present in almost 100% of the patients with clinical disease and are usually of the IgG class of immunoglobulins. In comparison, as many as 50% of the individuals with a similar degree of exposure to the antigen

also have precipitins, but remain asymptomatic (Fink 1973). There is considerable overlap in the titers of symptomatic and asymptomatic individuals; therefore, the titer itself is neither diagnostic nor prognostic.

With the exception of patients who have an asthmatic response to an ~~inhaled antigen, the role of serum antibodies is not clear and may represent a~~ natural immune response to an inhaled antigen. Elevated specific IgE antibody is only present in atopic individuals who have the immediate airway obstructive reaction characteristic of asthma in addition to the interstitial response.

The immunologic events responsible for the physiologic and anatomic abnormalities in acute and chronic hypersensitivity pneumonitis are recognized as complex. There is evidence both for and against an immune complex role. The presence of IgG precipitating antibodies in the majority of patients and the temporal relationship between antigenic exposure and the onset of acute illness (4-6 hours) are compatible with an immune complex and complement-mediated (Arthus-type) immunologic reaction.

In addition, lung biopsies obtained during acute reactions show infiltration of the alveolar walls chiefly with lymphocytes and plasma cells, while polymorphonuclear leukocytes and eosinophils occur only in modest numbers. Foamy macrophages containing C3 exist within the alveoli (Wenzel et al., 1971). In contrast to the findings in experimental Arthus reactions, there is no direct relationship between the antibody titer and the severity of acute reaction in patients with hypersensitivity pneumonitis. In some

patients, the precipitin titers may fall below the level of detection yet clinical sensitivity persists (Pepys 1969). Patients with chronic hypersensitivity pneumonitis may have low antibody levels in their sera, although their bronchoalveolar lavage fluids contain increased concentrations of IgG and, in many instances, increased titer of antibody against the presumed etiologic agent [Reynolds et al., 1977]. However, attempts to demonstrate immune complexes within alveolar lesions have been unsuccessful.

Additional evidence that IgG-mediated reactions are not solely responsible for hypersensitivity pneumonitis is a result of animal studies. In guinea pigs sensitized to produce antibodies but not cellular immunity, inhalation challenges produced a hemorrhagic alveolitis that was not morphologically compatible with farmer's lung (Richerson 1972). Moreover, it has not been possible to passively transfer the disease to monkeys with antibody-containing serum (Hensley et al., 1974). Thus, even though skin testing of individuals with pigeon breeder's disease with pigeon serum produces Arthus-reactions in 4-6 hours, current evidence suggests that these reactions, like the serum precipitins, are a consequence of antigenic exposure and unrelated to pathogenetic mechanisms.

Additional evidence for the participation of humoral factors in hypersensitivity pneumonitis, however, includes demonstrations that the alternate pathway of complement fixation may be activated by spores of thermophilic actinomycetes and other antigens (Edwards et al., 1974). This pathway may play a direct role in the genesis of the inflammatory response within the lung by releasing mediators or may interact with the circulating antibody and immune complexes to induce lesions.

Recent evidence suggests a role for cell-mediated immune responses in the pathogenesis of hypersensitivity pneumonitis. Biopsies show lymphoid cell infiltrations and granuloma formation suggesting this type of immune response. Lymphocytes from patients with pigeon breeder's disease or farmer's lung may produce macrophage migration inhibition factor when exposed to the appropriate antigens in vitro; blood lymphocytes from symptomatic pigeon breeders may respond to pigeon serum antigens with increased thymidine incorporation and lymphocyte transformation (Fink et al., 1975; Hansen & Penny 1974; Moore et al., 1974). Analyses of peripheral lymphocyte subpopulations in patients with hypersensitivity pneumonitis have demonstrated reduced circulating T cells in those with active disease (Flaherty et al., 1976). Analyses of lavage lymphocyte subpopulations of patients with chronic hypersensitivity pneumonitis have demonstrated a significant increase in absolute numbers as well as antigen-reactive T cells when compared with blood (Reynolds et al., 1977).

#### Animal models

Animal models have been widely used to study the pathogenesis of hypersensitivity lung disease.

Humoral aspects have been studied in guinea pigs sensitized and exposed by intratracheal administration of ovalbumin. The animals developed a hemorrhagic pneumonia, although in 24 hours the cellular population changed to mononuclear cells including predominately T cells (Bernardo et al., 1979). Passive transfer studies using antipigeon serum in monkeys followed by inhalation challenge also induced a hemorrhagic pneumonia characterized by the

deposition of immune complexes and complement (Hensley et al., 1974). Rabbit lesions due to the installation of Micropolyspora faeni spores into the lung have been shown to be complement-dependent. No lesions developed if complement was depleted (Wilson et al., 1981). While these models demonstrate that humoral factors may induce pulmonary disease after appropriate challenge, the disease is generally unlike human hypersensitivity pneumonitis.

Animal data are also compatible with a cell-mediated reaction in hypersensitivity pneumonitis. Guinea pigs with delayed hypersensitivity to protein antigens respond to inhalation challenge with the production of interstitial infiltrations that resemble acute hypersensitivity pneumonitis in humans (Ratajczak et al., 1980; Richerson 1972). Similar lesions have been induced in monkeys by passive transfer of cells from donors sensitized to pigeon serum (Hensley et al., 1974). Antibodies and complement were not detectable in the pulmonary lesions of these primate recipients. Although these observations strongly suggest that cell-mediated immunity plays a role in the pathogenesis of hypersensitivity pneumonitis, it does not exclude the possibility that a combination of immune complex and complement along with cell-mediated reactions are necessary for production of clinical hypersensitivity pneumonitis in exposed individuals.

Most patients with hypersensitivity pneumonitis have demonstrable precipitating antibodies and cellular immune reactions to an offending antigen. Thus, it is likely that several types of immune reactions are important in the pathogenesis of the disease.

### 2.3 Clinical and Epidemiological Review

The nature and extent of the clinical features occurring in hypersensitivity pneumonitis depend primarily on the clinical form of the disease.

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#### (a) Acute Form

The acute form of hypersensitivity pneumonitis is characterized clinically by chills, fever, cough, breathlessness without wheezing, and malaise occurring 4-10 hours after antigen exposure (Fink et al., 1968). There is some correlation between the severity of the acute episode and magnitude of the antigenic challenge; however, immunologic responsiveness also influences the severity of an attack. In general, an acute attack subsides in 18-24 hours.

The classic response to antigen exposure results in maximum changes 4-8 hours after exposure (Schlueter 1974). Changes are primarily restrictive with a decrease in FVC, FEV<sub>1</sub> and total lung capacity (TLC). There is little change in flow rates, but small airway obstruction may be demonstrated. There is a decrease in static compliance, and dynamic compliance becomes abnormally frequency-dependent. Changes in the small airways result in nonuniform ventilation distribution, and, in turn, disturbance in ventilation-perfusion relationships. Hypoxemia and impaired diffusing capacity are manifestations of this mismatching (Schlueter et al., 1969). Hypoxemia may also be caused by redistribution of blood flow, with resulting ventilation-perfusion inequality, or be secondary to intrapulmonary shunting of blood.

Several other patterns of response are seen. The 4-6-hour late reaction can be preceded by an immediate asthmatic reaction with decrease in  $FEV_1$  and expiratory flow rates. These early changes resolve in 1-2 hours. In atopic subjects, an acute asthmatic response (with wheezing and evidence of airflow obstruction on standard testing) may occur within minutes after antigen inhalation (Pepys 1969; Schlueter 1974). The attack may subside with or without treatment, but 4-8 hours later the acute restricted response described above will occur. Patients with bronchopulmonary aspergillosis also have this dual response. By contrast, however, their late response is also characterized by an obstructive pattern on standard physiology testing.

In the majority of patients with the acute disease form, particularly with exposure avoidance, pulmonary function returns to normal within a few days to weeks. Even with repeated acute attacks, if the exposure is not intense or frequent, pulmonary function may remain normal between exposures.

(b) Subacute form

A small number of patients shows a more insidious form of disease resembling a progressive chronic bronchitis with productive cough, dyspnea, easy fatigue, and weight loss (Fink 1973; Fink et al., 1968; Pepys 1969). Both restrictive and obstructive defects in pulmonary function can be observed; the former, however, predominate along with a decrease in static lung compliance and diffusing capacity. Hypoxemia, although only mild at rest, may show a substantial worsening with exercise. Long-term avoidance of exposure and administration of corticosteroids usually results in resolution of these functional abnormalities, though resolution takes longer than in the acute form.

(c) Chronic form

Prolonged exposure to an organic dust causing hypersensitivity pneumonitis can lead to the gradual development of disabling respiratory symptoms with irreversible physiologic changes (Fink 1973; Pepys 1969).

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~~Pulmonary fibrosis is the predominant finding, particularly as seen in~~ farmer's lung or in patients with chronic low-level exposure to antigens. These patients have progressive restrictive impairment, a diffusion defect, hypoxemia, and decreased lung compliance. Pulmonary fibrosis may progress, even without further exposure and despite corticosteroid therapy, eventually resulting in respiratory failure.

A few patients with the chronic form of the disease have also shown signs and symptoms of obstructive disease (Schlueter et al., 1969). Physiologic studies have shown diminished flow rates, hyperinflation with markedly elevated residual volume, decreased diffusing capacity, and a loss of pulmonary elastic recoil pressure suggestive of emphysema. In these cases, biopsy specimens have revealed an obstructive bronchiolitis with distal destruction of alveoli. Avoidance of exposure (even for prolonged periods) and corticosteroid therapy afford only minimal improvement; the disease tends to be progressive (Fink et al., 1968).

In the chronic form of the disease, the symptoms are primarily respiratory and consist of progressive shortness of breath, leading to pulmonary disability. There may be associated anorexia and weight loss with mucopurulent sputum, but acute episodes do not occur (Fink et al., 1968).

(d) Laboratory evaluation

Blood studies. A polymorphonuclear leukocytosis of up to 25 000/mm<sup>3</sup> (25.0 x 10<sup>9</sup>/L) with a shift to young forms is the usual finding in the acute phase of hypersensitivity pneumonitis; it resolves with recovery and is not evident between attacks. Occasionally, eosinophilia of up to 10% may be seen in the sensitized patient.

There is generalized elevation of immunoglobulin levels, except for IgE. Rheumatoid factor tests are positive in 65% of the patients during periods of illness, but become negative after prolonged avoidance.

(e) Radiologic studies. Chest X-ray studies of patients with hypersensitivity pneumonitis can be normal if recurrent episodes are infrequent. Usually, however, there are detectible fine sharp nodulations and reticulations with general coarsening of bronchovascular markings. During an acute attack, soft, patchy, ill-defined diffuse parenchymal densities, which tend to coalesce, may be seen in both lung fields. Chronic or end-stage disease may present as diffuse fibrosis with parenchymal contraction or even honeycombing (Unger et al., 1973).

(f) Pulmonary function studies. A number of pulmonary function abnormality patterns can occur, depending on the clinical form of hypersensitivity pneumonitis (Pepys 1969; Schlueter 1974).

During acute episodes, the most common response occurs 4-8 hours after exposure to the offending antigen. There is a decrease in FVC and FEV<sub>1</sub>; the ratio between these two parameters remains constant. There is little change

in expiratory flow rates. A decrease in compliance, indicating increased lung stiffness, and a fall in diffusion capacity may also occur during acute episodes. Determination of arterial blood gases usually demonstrates hypoxemia which is accentuated by exercise. Closing volumes may also increase and maximal mid-expiratory flow rates decrease. As the attack subsides, these ~~abnormalities as well as hypercapnia may be found during asymptomatic phases.~~

In patients with the more chronic forms of hypersensitivity pneumonitis, less reversible pulmonary function abnormalities may be detected. In the subacute form, a more persistent restrictive impairment and diffusion defect may be demonstrated during exposure and even for some time after cessation of contact with the antigen (Schlueter et al., 1969).

The most marked physiologic alterations have been found in patients with the chronic form of hypersensitivity pneumonitis readily studied in individuals with pigeon breeder's disease (Fink et al., 1968) or farmer's lung. A severe restrictive impairment with a moderate-to-marked diffusion defect has been shown to persist in some of these patients and may be physiologically correlated to the pulmonary fibrosis demonstrable on chest X-ray and lung biopsy.

Other individuals with chronic hypersensitivity pneumonitis may demonstrate poorly reversible and progressive obstructive disease with hyperinflation and elevation of residual volume. A loss of pulmonary elasticity with increased static compliance may be detected in these individuals (Schlueter et al., 1969). Some of this latter group may also have decreased diffusion capacity. These findings may correlate with biopsy evidence of obliterative bronchiolitis and emphysema (Fink et al., 1968).

(f) Lung lavage. Lung lavage has become a tool of investigation of a variety of pulmonary problems of obscure nature. The findings of predominantly lymphocytes in lavage fluid suggests the diagnosis, among others, of hypersensitivity pneumonitis. More sophisticated tests of the lymphocyte reactivity may point to pigeon breeder's disease as being present (Moore et al., 1980). The future of this approach is still not clear.

(g) Immunologic studies. The characteristic immunologic feature of hypersensitivity pneumonitis is the occurrence of serum precipitating antibodies against the specific organic dust antigen (Barboriak et al., 1965; Fink 1973; Pepys 1969). Agar gel diffusion techniques with a suspect antigen and the patient's serum can be used to demonstrate antibodies in most ill individuals. However, these tests must be evaluated in light of clinical findings since up to 50% of similarly exposed, but asymptomatic individuals, may also have moderate-to-high titers of serum precipitating antibodies. The antibodies in symptomatic and asymptomatic individuals belong largely to the IgG class of immunoglobulins, but IgA and IgM antibodies have also been detected in these sera by radioisotope techniques.

Epidemiologically, the incidence of hypersensitivity pneumonitis is not usually known. Patients with this disease may be categorized under interstitial lung, occupation airway or inhalation diseases.

There is little information available regarding a relationship between antigens, exposure and disease. In a given population, similarly exposed to a potential sensitizing inhalant agent, the number of individuals with

detectable disease has ranged from 3-15% (Christensen et al., 1975; Moore et al., 1974). Yet, up to 50% of exposed but asymptomatic individuals in similar environments have detectable humoral or cellular immune responses to the antigen without clinical evidence of disease. Thus, some other unknown factors are important in the pathogenesis of hypersensitivity pneumonitis and

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Genetic factors. Recent evidence has demonstrated that pigeon breeder's disease is not associated with genetic immunologic responsiveness, as determined by HLA histocompatibility typing of ill and well pigeon breeders. Other evidence, however, has suggested that farmer's lung or pigeon breeder's disease may be under genetic control, with an increased frequency of the HLA haplotype in ill individuals (Allen et al., 1975; Flaherty et al., 1975).

Pulmonary inflammation. Recent evidence, using animal models of hypersensitivity pneumonitis, suggests that some inflammatory event must occur in the lung in addition to recurrent antigen inhalation exposure for disease to develop. Animals chronically exposed to pigeon antigens demonstrated an immune response, but no pulmonary inflammation was evident until an agent such as BCG or carageenan was administered (Moore et al., 1975). Such agents, including infectious organisms, may stimulate the immune response by adjuvant action or by enhancement of antigen absorption through inflamed mucosa.

Toxic factors. The induction, progression and severity of hypersensitivity pneumonitis may be related to a variety of toxic exposure. Possible toxicants include tobacco smoke, air pollution, and industrial exposure. Allen and coworkers (1975) have linked the occurrence of pigeon

breeder's disease with the use of hexachlorobenzene as a disinfectant in pigeon lofts. The factors may enhance absorption of antigens as a result of pulmonary inflammation. They may also increase local immune responses or may act systematically as adjuvants.

Immunologic abnormalities of the host. Recent evidence suggests that immunoregulatory defects in which suppressor T cells are nonfunctional may be important in the pathogenesis of the lesions of hypersensitivity pneumonitis (Keller et al., 1982). Failure in immunoregulation may allow the humoral antigen- antibody complex or cell-mediated immune response to progress with resultant pulmonary inflammation.

#### Prevalence statistics

Grant and coworkers (1972), in a study of 655 farm workers in Scotland, found the prevalence of farmer's lung to range from 2.3-8.6% in three different counties. Staines and Froman (1961), in another British study, estimated the prevalence of farmer's lung in two communities to range from 0.5-1% of the farm population. Morgan and coworkers (1973) studied 93 farmers in an area endemic for farmer's lung and showed that nine (9.6%) had typical clinical histories of the disease. A study in the USA surveyed 471 individuals associated with farming or dairy production in Western Wyoming (Madsen et al., 1976). A history typical of farmer's lung syndrome was found in 14 (3.9%) individuals. The prevalence of farmer's lung in this community was comparable to the UK studies.

There is little doubt that farmer's lung is an important occupational illness in farmers in the UK and USA, but the diagnosis may be overlooked due to lack of patient or physician awareness. Recently, 1045 dairy farmers in Central Wisconsin were surveyed for precipitins to a panel of antigens including thermophilic actinomycetes, Aspergillus and pigeon serum (Marx et al., 1978). ~~Of the group, 8.5% had precipitating antibodies to one or more of~~ the thermophilic actinomycetes, while 0.4% had precipitins to one of the aspergilli. All of the individuals with precipitins were further evaluated. A positive history of farmer's lung was given in 36% and 10% had a questionable history.

Based on these findings, there is potential development of approximately 32 cases of farmer's lung per 1000 in dairy farmers in the USA. This would result in 4800 cases in the State of Wisconsin alone, a figure far exceeding the frequency of many other diseases. This high estimated prevalence is particularly alarming because these patients are at risk of developing chronic irreversible lung damage.

Bagassosis has a worldwide distribution and occurs wherever sugar cane is processed. Cases have been reported from Puerto Rico (USA), Cuba, India, Italy, Peru, and the United Kingdom (Pepys 1969). Cases have also been identified in nonoccupationally exposed individuals such as those using the material as a garden mulch, housewives residing in homes several miles downwind from sugar cane fields and processing areas, and employees working in air-conditioned offices at or near sugar-cane processing areas.

Pigeon breeder's disease has been estimated to occur in 6-15% of individuals who raise pigeons for a hobby (Christensen et al., 1975; Fink et al., 1972). There are approximately 75 000 breeders in the USA and 250 000 in

Belgium; therefore, if the estimated prevalence is correct, as many as 10 000 to 35 000, respectively, of these individuals could develop irreversible lung damage in those two countries alone.

Studies of several office worker populations exposed to contaminated air cooling systems have demonstrated a prevalence of hypersensitivity pneumonitis, 15% in one outbreak [Banaszak et al., 1970] and less than 1% in another [Arnow et al., 1978].

In an unpublished study of more than 250 veterinarians, 100 animal caretakers and a nonexposed comparison population, no instances of a history of hypersensitivity pneumonitis due to animal antigens were found by assay of IgG-IgM specific antibodies using both immunodiffusion and counter-immunoelectrophoresis. Very few of the subjects had reactions to Aspergillus, Alternaria or thermophilic actinomycetes.

Thus, although specific prevalence and incidence data are not available for each type of hypersensitivity pneumonitis, it is known that the disease represents a serious health problem in many occupations. It is also believed to occur more frequently in home and office environments than has been recognized (Fink 1971).

Removing the affected worker from occupational exposure, a step frequently quite disruptive to the individual, is the most effective control measure for abnormalities associated with hypersensitivity pneumonitis. Prevention of the disease through lowering antigen levels in the work environment is a more satisfactory approach. In a few instances, such as in the lumber industry, exposure of workers to potentially problematic dusts has

been prevented by operational changes. For example, maple bark stripper's disease has been eliminated by altering handling of the logs in order to prevent growth of the organism. High dust concentrations occurred in the wood room, especially in winter, and it was shown that most of the dust material consisted of clouds of spores of Cryptostroma corticale (Wenzel & Emanuel, 1967). ~~The changes instituted included eliminating the saw area by installing debarking drums, spraying drums continuously with water containing a detergent, isolating the chippermen from the wood room with a glass positive-pressure room, and cautioning the workroom crew against spending excessive time in areas of high dust concentrations. These changes resulted in a dramatic decrease in spore counts during the winter, and since that time there have been no further cases of maple bark disease in the particular plant.~~

Attempts to prevent bagassosis have been made by drying the material or by treatment with propionic acid to prevent growth of microorganisms (Lacey 1974). Bagassosis has also been reported to have been eliminated from a Louisiana paper mill by process changes (Lehrer et al., 1978). These involved both storage and processing modifications which retarded microbial growth and reduced the generation of organic dust.

Immediate practical measures of hypersensitivity pneumonitis prevention and control include educating individuals and industries at risk. Workers exposed to incriminated organic dusts must be made aware of potential hazards. Appropriate industries must be encouraged to reduce sensitizing and challenging exposures. Industrial physicians, public health officials, primary care physicians, and consultants must be alerted to the importance of prevention as well as diagnosis and treatment of this group of diseases.

The limited current control of hypersensitivity pneumonitis is primarily confined to manipulations of an ill individual's environment. Environmental factors have been clarified by studies of the causative agents and their sources, and individual patients have benefited greatly by these studies. Of more economic and epidemiologic importance, however, would be predictive and preventive measures affecting whole environments and communities of workers, which would result from an increased understanding of sensitizing events and host factors. Further research is required to establish the knowledge necessary for the design of feasible preventive programs and the maintenance of a healthy, stable work force in relevant environments. With the substantial volume of lung tissue involved and the chronic nature of the alveolar hypoxia chronic, pulmonary hypertension develops. Chronic and sustained pulmonary hypertension leads to right ventricular enlargement and ultimately to right ventricular failure. Respiratory failure, as a result of extensive destruction and fibrosis of lung tissue, may be seen in the end stages of chronic, progressive lung disease.

#### Treatment

The major therapy for hypersensitivity pneumonitis is avoidance, the same as for all allergic disorders once the offending antigen is discovered. Since many of these disorders are occupational, and the antigen may be recognized, the use of masks with filters capable of removing the antigen, appropriate ventilation of working areas, or changing occupations if necessary (Fink 1973; Pepys 1969).

In the acute or subacute forms of hypersensitivity pneumonitis, when avoidance cannot be quickly achieved, drug therapy can be instituted. Corticosteroids are the drug of choice and will abort and prevent the episodic illness. Antihistamines and bronchodilators have no effect. If the corticosteroids are administered while avoidance is practised, ~~reversibility~~ of the clinical and laboratory abnormalities is usually possible. Immunotherapy, as used for treatment of atopic diseases such as asthma and allergic rhinitis, is contraindicated in hypersensitivity pneumonitis because of the possibility of immune complex vascular damage.

#### 2.4 Research priorities

A major priority in research efforts should be the determination of the pathogenesis of these disorders. Animal models, sophisticated patient studies and purification of relevant antigens are of importance in elucidating the pathogenesis of hypersensitivity pneumonitis.

Animals models would also be useful in determining which organic dusts can sensitize the defense mechanism of the lung, as well as providing a screening mechanism, to determine the pathogenicity of dusts.

The prevalence and natural history of these diseases should be determined, perhaps by international cooperative efforts. The initial studies could be carried out in well-defined populations. Quantitation of antigen loads, as well as disease prevalence, should be determined.

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### 3. BYSSINOSIS<sup>1</sup>

#### 3.1 Introduction and Historical Considerations

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In the original planning of this book, byssinosis was not included in view of the fact that a WHO Study Group met on this subject (WHO, 1983) and produced an elaborate report. However, it was later on found advisable to include this brief review to enable those who have no access to the WHO report to obtain an overview covering one of the most important diseases caused by vegetable dusts.

Byssinosis has been recognized as an occupational respiratory disease for more than 120 years. Epidemiologically, it occurs among the workers exposed to airborne dusts of cotton, flax and soft hemp. In its early stages, it is characterized by symptoms of respiratory tightness and cough, particularly upon return to exposure from holidays. Respiratory disability with emphysema and right-sided heart failure in advanced byssinosis occur after prolonged exposure to cotton. At present, byssinosis is included in the lists of notifiable and compensable occupational diseases in many countries.

Knowledge about the disease has an interesting historical evolution. In the year 1700, Ramazzini devoted a chapter to the "Diseases of those who pick or hatchel flax, hemp and silk". In 1831, Kay described what he called "spinners phthisis" in the Manchester cotton industry as commencing with "distressing pulmonary irritation from the dust and filaments which he

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<sup>1</sup>By El Batawi, M.A.

inhales" which was associated with "define and obscure sensation of uneasiness beneath the sternum". These "symptoms become gradually more severe; the cough is at length very frequent, accompanied with little or no expectoration" (Kay, 1831).

Thackrah (1832) recognized the disease as similar to that which he experienced among flax-workers, and observed a marked reduction in vital capacity of advanced cases. He attributed emphysema observed in the lungs of workers affected by the disease for life time to chronic "dry bronchitis". The disease was given its name "byssinosis" by Oliver in 1902 (meaning fine fibers in the lungs). This term did not come into common use until about 1940 (Meiklejohn, 1963).

Prausnitz, in 1936, published an extensive account on the disease containing the results of his epidemiological and experimental studies. He and his co-workers presented evidence of the content of a histamine-like substance in cotton dust, but doubted any pronounced role of this substance in causing the disease. On the other hand, a substance or group of substances contained in the protein fraction was regarded as the probable cause of the disease.

Disabling byssinosis became compensable in the United Kingdom for the first time in 1941 (Meiklejohn, 1963). Extensive research in all aspects of this disease started some thirty years ago. Following a field study by Schilling in the early fifties of cardiovascular diseases among workers in the cotton mills, he revealed that a substantial proportion of the deaths attributed to cardiovascular mortality were not primarily due to heart disease but represented a terminal event in fatal emphysema caused by byssinosis. He

records (1956): "Although we had been misled by mortality statistics into a study of cardiovascular disease, it had not been fruitless, it turned our attention to byssinosis, which was generally thought to be a diminishing and unimportant problem in Lancashire."

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Earlier, a classification of byssinosis into grades I and II was suggested and tested. Complete dependence on symptoms and the lack of objective criteria for the diagnosis of byssinosis including the absence of specific radiographic changes in the lungs made it difficult to obtain unanimous agreement on diagnosis. With the introduction of a systematic questionnaire, Schilling's classification prevailed (1956):

Grade 0: no symptoms; Grade 1/2: occasional Monday symptoms; Grade I: chest tightness and/or cough; Grade II: symptoms extending to other days of the week, and Grade III: advanced obstructive pulmonary manifestations.

Roach and Schilling (1960) following extensive clinical and environmental measurement of dust exposure suggested  $1 \text{ mg/m}^3$  of air as a safe level of exposure and attributed the symptoms to a protein containing fraction contained in the plant debris contained in the airborne cotton dust. Exposure to cotton dust, even among the workers unaffected by byssinosis, was found to cause acute reduction in the ventilatory capacity during the work shift. This reduction was reversible. Cases of byssinosis, in general, showed more marked drop in ventilatory capacity (McKerrow et al., 1958).

Many studies were conducted in the 1960s in different countries on byssinosis among cotton and flax workers. Several of these studies demonstrated high prevalence rates of byssinosis in cotton ginning and textile industries and in flax processing (Batawi et al., 1964a, and Batawi & Hussein,

1964). The major areas of investigation in the 1970s and 1980s were addressed to the pathogenesis of byssinosis. In addition, a large number of epidemiological studies were conducted, including dust evaluation and clinical observation. These studies helped in better understanding of the nature of this disease and its relationship to the duration of exposure at different concentration levels and the various components of the airborne dust.

### 3.2 Pathology and Pathogenesis

There have been few systematic studies of the pathological changes in the lungs of textile workers with byssinosis. Several case reports from the earlier literature, as well as some more recent observation, were reviewed by Schilling in 1956 with only one additional report since then by Edwards and colleagues (1975). Pathological changes in advanced byssinosis are similar to those found in chronic bronchitis and emphysema. In particular, there is no evidence that long-term textile dust exposure leads to fibrosis of the lungs. The loss of elastic recoil of the lungs in older workers indicates that at least some of these workers suffer from damage to the elastic structure of the lung parenchyma, similar to that in emphysema from other causes. However, in some reported cases, only minor emphysema was found at autopsy of men who died after having been totally disabled with dyspnea and cough during the last years of their life. It is conceivable, then, that the "irreversible" ventilatory insufficiency in these workers is caused, at least in part, by widespread small airway obstruction rather than by structural damage to the lung parenchyma (Guyatt et al., 1973). The fact that the ventilatory capacity of these workers usually cannot be increased significantly with strong-acting bronchodilator drugs such as isoprenaline hydrochloride or sulfate (INN) (or in the USA, isoproterenol) shows only that the small airway obstruction cannot

be readily reversed with drugs which relax smooth muscle. Permanent pathological damage in the lungs starts with thickening of the mucosal lining of the bronchi and the bronchioles and their gradual narrowing caused by the dust, eventual chronic bronchitis and emphysema. Microscopically, there is hyperplasia of the mucous glands and smooth muscle hypertrophy in the lower bronchi. Interstitial tissue may be diminished and when emphysema is present, it is that of the centrilobular type (Edwards et al., 1975).

Pathogenesis of byssinosis has been the subject of extensive investigation in many parts of the world, particularly in Great Britain, Egypt, Sweden, the United Kingdom and the United States of America. There are worldwide studies showing that dusts of cotton, flax, soft hemp and sisal cause byssinosis. For many years, epidemiological studies of workers exposed to sisal dust in the United Kingdom and Africa gave no evidence to suggest that this dust caused byssinosis (Gilson et al., 1962). In one study in Tanzania (Mustafa et al., 1978), workers heavily exposed to sisal dust were found to have the characteristic symptoms of byssinosis.

The pathogenesis in byssinosis is not as yet certain. There is, however, some evidence that a primary toxic reaction from a histamine-releasing substance may account for the acute signs and symptoms of byssinosis (Antweiler, 1960; Hitchcock et al., 1973). On the other hand, there is growing evidence supporting the role of endotoxins in the causation of byssinosis (Rylander, 1981; Delucca & Palmgren, 1986).

The evidence in favor of histamine-release from mast cells in the lungs as a principal mechanism (Bouhuys & Lindell, 1961) may be summarized as follows:

- (a) Cotton and other textile dusts cause chest tightness from bronchoconstriction in most healthy persons without previous sensitization.
- (b) The somewhat delayed effect (a few hours) of the cotton dust or its extracts in human volunteers is consistent with an indirect effect, which is consistent with the release of a stored mediator.
- (c) Textile dusts and bracts extracts release histamine from human lung tissue without previous sensitization; the time course of histamine-release, in vitro, is consistent with the time course of in vivo responses (Noweir, 1981).
- (d) The decreasing response to cotton dust observed after a first exposure to cotton dust (after a holiday interruption) corresponds to a similar phenomenon observed after administration of known histamine-releasing agents (Antweiler & Felberg, 1975).
- (e) In purified cotton, the causative agent is absent and no byssinosis is observed among the workers exposed to airborne dust in processing medical cotton (Batawi & Shash, 1962).

It has also been suggested that the symptoms of byssinosis are caused by endotoxins in airborne cotton dust from the Gram-negative bacteria which are proven to be contained in airborne dust, particularly when cotton had been stored for sometime before processing. Evidence was discussed first by Pernis and co-workers (1961) who found that rabbits exposed to endotoxins by inhalation on two consecutive days had more dyspnea on the first day than the

second. This was presumably due to the well-known phenomenon of tolerance to the endotoxins and is reminiscent of the "Monday effects" of byssinosis. They also explained that "at least some of the histamine release" in vitro and in vivo with cotton dust exposure may be caused by endotoxins. ~~Further evidence~~ was shown by Rylander and Snella (1976) who demonstrated that in guinea-pigs exposed to cotton dust extracts, a correlation was found between the increase in number of leukocytes in the airways and the number of Gram-negative bacteria as well as the content of endotoxins in the dusts. Epidemiologically, it has been shown that airborne bacteria, the protease content of airborne dust in 21 cotton spinning mills in Lancashire correlate significantly with the prevalence of byssinosis symptoms (Cinkotai & Whitaker, 1978). Rylander and colleagues (1979) also showed similar correlations in the USA.

When byssinosis and its advanced stages are taken as a whole, the evidence available so far suggests:

- (a) that a pharmacologically active principle present in the airborne cotton dust causes the liberation of histamine causing bronchoconstriction; and that the dust also contains endotoxins in the cell wall of Gram-negative bacteria which also have the ability to liberate histamine as well as to cause inflammation in the bronchi. The two factors are not mutually exclusive and may be acting together in causing the chest tightness in byssinosis upon return from holidays;
- (b) these mechanisms do not explain the long-term effects of the dust which are chronic obstructive respiratory manifestations that

down to the deep respiratory passages caused by the dust particles of cotton, flax, soft hemp and sisal. Many of the workers exposed to freshly hand-picked cotton dust, that does not contain much plant debris, do not show the typical symptoms of chest tightness on return from holidays or work interruption. However, there is a significantly high prevalence of chronic obstructive pulmonary disease among the workers exposed to high dust concentration for some years (Batawi, 1969)

### 3.3 Clinical and Epidemiological Review

Byssinosis differs from chronic obstructive pulmonary disease (COPD) in its being associated with typical symptoms of notable chest tightness and/or cough in the first day (or days) of exposure to the causative airborne dusts after return from weekend holidays or a seasonal interruption of the dusty operations. Unlike the mill-fever, the symptoms are essentially pulmonary without elevation of body temperature, with the exception occasionally, of young workers exposed for the first time (author's observation, unpublished). These symptoms are called "Monday symptoms" in western countries. As mentioned earlier, the disease was given different clinical grading by Schilling:

Grade 0: no symptoms;

Grade 1/2: occasional chest tightness and/or shortness of breath on the first day of working week;

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Grade I: chest tightness and/or shortness of breath on every first day of the working week;

Grade II: symptoms of grade I extending to other days of the week; and

Grade III: grade II symptoms accompanied by evidence of permanent loss of lung function.

This classification was associated with a parallel classification of physiological changes in ventilatory capacity as measured by the forced expiratory volume (one second) ( $FEV_1$ ) which demonstrated that there was a drop in  $FEV_1$  during the working shift of exposed workers that was higher among those having the above symptoms. This grading showed a number of imperfection when applied in different countries, particularly where cotton is grown, hand-picked and processed in its fresh state without prolonged storage (with less likelihood of microbiological growth). In these instances, the exposed workers complained of eye and upper-respiratory tract irritation and cough on exposure to cotton dust. No variation from day-to-day was mentioned by the workers, although when asked some complained that these symptoms occurred during the last day, rather than the first, of the working week (Batawi, 1969).

Exposure to retted flax dust invariably caused Monday symptoms that would last for more days if the period of holiday before return to work, after seasonal interruption, was longer. Retted flax is subject to extensive growth of microorganisms which consume the carbohydrate binding material of flax fibers, thereby facilitating flax combing into long fibers for spinning. In examining a representative sample of the total population exposed to flax, including those who retired by age or illness and stayed in their homes, in an Egyptian village that entirely depended for living on flax growing and manufacturing, Batawi and Hussein (1964) observed that advanced pulmonary disability due to obstructive pulmonary disease was relatively much less among flax workers than cotton workers. They wrote "unlike the difficulty experienced by one of us (Batawi & Abdel-Salam, 1961) in previous studies among cotton workers, where in many cases the diagnosis of byssinosis was difficult to establish, the symptomatology in flax workers was more obvious and the diagnosis was easier to make". They add, ... "many cotton workers complained of tightness and cough related to an elevation of the dust concentration in the work environment during the week, as in cleaning, rather than to a return from holiday ... In flax, however, the symptoms of byssinosis were easier to elicit and the tightness and/or dyspnea occurred more severely on Mondays, even though the subjects were quite appreciably 'disabled' by advanced obstructive respiratory disease".

Exposure to high concentrations of cotton dust above  $10 \text{ mg/m}^3$  air for more than 10 years was found to be associated with chronic nasal sinusitis in a significant magnitude (Batawi et al., 1964b).

For these reasons the WHO Study Group (1983) proposed the following classification of clinical manifestations and lung function changes in exposure to vegetable dusts causing byssinosis or asthma.

Table 5. Classification of clinical manifestations and lung function changes in respiratory disorders from exposure to vegetable dusts causing byssinosis or respiratory tract irritation

Classification	Symptoms
Grade 0	No symptoms
<u>Byssinosis</u>	
Grade B1	Chest tightness and/or shortness of breath on most of first days back at work
<del>Grade B2</del>	<del>Chest tightness and/or shortness of breath on the first and other days of the working week</del>
<u>Respiratory tract irritation (RTI)</u>	
Grade RTI 1	Cough associated with dust exposure
Grade RTI 2	Persistent phlegm (i.e., on most days during 3 months of the year) initiated or exacerbated by dust exposure
Grade RTI 3	Persistent phlegm initiated or made worse by dust exposure either with exacerbations of chest illness or persisting for 2 years or more
<u>Lung function</u>	
1. <u>Acute changes:</u>	
No effect	A consistent <sup>a</sup> decline in FEV <sub>1.0</sub> of less than 5% or an increase in FEV <sub>1.0</sub> during the work shift
Mild effect	A consistent <sup>a</sup> decline of between 5-10% in FEV <sub>1.0</sub> during the work shift
Moderate effect	A consistent <sup>a</sup> decline of between 10-20% in FEV <sub>1.0</sub> during the work shift
Severe effect	A decline of 20% or more in FEV <sub>1.0</sub> during the work shift
2. <u>Chronic changes:</u>	
No effect	FEV <sub>1.0</sub> <sup>b</sup> - 80% of predicted value <sup>c</sup>
Mild to moderate effect	FEV <sub>1.0</sub> <sup>b</sup> - 60-79% of predicted value <sup>c</sup>
Severe effect	FEV <sub>1.0</sub> <sup>b</sup> less than 60% of predicted value <sup>c</sup>

<sup>a</sup>A decline occurring in at least three consecutive tests made after an absence from dust exposure of two days or more.

<sup>b</sup>Predicted values should be based on data obtained from local populations or similar ethnic and social class groups.

<sup>c</sup>By a pre-shift test after an absence from dust exposure of two days or more

Epidemiologically, byssinosis has been investigated worldwide. In the East-European countries, the Monday tightness has not been described, but rather irritation due to dust exposure and in prolonged exposure, the occurrence of chronic obstructive pulmonary disease. Epidemiological observations has been satisfactorily supportive of an exposure/effect, response relationship. This has facilitated the establishment of recommended exposure limits (less than  $0.2 \text{ mg/m}^3$  air) although, in a few instances, it has not been possible to find definite evidence of a threshold dust concentration below which symptoms or functional changes do not occur. For an elaborate discussion of epidemiological findings and recommended exposure limits for cotton and flax, the reader may refer to the report of the above-mentioned WHO Study Group (WHO, 1983).

#### 3.4 Research Priorities:

Research is still needed in a number of areas that are relevant to the prevention of disease and disability caused by the dusts under consideration. These areas may be summarized as follows:

- (a) Research in pathogenesis appears to be an attractive field in view of the types of symptoms in byssinosis. The endotoxin theory and that of pharmacological histamine liberation by other component(s) in the airborne dusts are, until today, subject to further research.
- (b) Prospective studies are needed to follow up workers exposed to the various causative dusts in order to observe whether there is any sequence in events in developing byssinosis. These studies would

require careful observation of the dust exposure, constituents of the airborne dust, biological activity, immuno-toxicity in animal models as well as observation and early detection of health effects in exposed workers including cellular changes, histamine levels in blood and tissues, and the release of lysosomal enzymes from polymorphonuclear cells. Such parameters may not only clarify the mechanism of action but also serve, when established, as manifestations of susceptibility and for early detection of reversible changes.

- (c) Environmental evaluation and control: the efficacy of modern methods of dust suppression by ventilation and enclosure should be evaluated in view of the fact that some individuals were proven to be more susceptible than others even in very low levels of exposure. Direct reading equipment of dust concentration are not as yet available for use by primary health care workers in small-scale industries of cotton and flax. Such equipment, as available for evaluation of mineral dust concentration, would be most useful in monitoring of the work environment and advising employers on the need for control measure. Portable equipment for the evaluation of forced expiratory volume of the workers exposed are presently available. However, there is a need for their periodic calibration to ensure reliability of measurements. There is also a need for their production on a large scale.

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#### 4. CHRONIC OBSTRUCTIVE PULMONARY DISEASES

##### 4.1 Pathology and Pathogenesis<sup>1</sup>

It has become increasingly apparent that vegetable and other organic dusts are associated with symptoms of acute and chronic pulmonary disease. The most frequently reported example has been grain dust exposure in which cough, wheezing and chronic bronchitis have been demonstrated to occur with increased frequency. Other dusts reported to have similar consequences include jute, hemp, sisal, tea, tobacco and the various components of dust in animal confinement centers (Becklake, 1980; Becklake et al., 1980; Castellan et al., 1981; Cotton & Dosman, 1978; doPico, 1979; doPico et al., 1977; Dosman et al., 1979; Jones et al., 1982; Katila et al., 1981; Nicholls & Skidmore, 1975; Valic & Zuskin, 1971; Valic & Zuskin, 1972; Valic et al., 1976; Warren & Manfreda, 1980; Zuskin & Valic, 1973;).

Unlike the pathologic changes of chronic bronchitis associated with the inhalation of cotton dust (Rooke, 1981), the pathologic changes occurring in the lung as a result of exposures to these other dusts have not been described. It is known, however, that pulmonary function tests, when measured, have revealed airflow obstruction indicating that the result of these exposures is obstructive airways' disease. These exposures may result in

<sup>1</sup>By Hunninghake, G.W. & Wanzek, S.R.

obstructive airways disease. These exposures may result in airways disease by multiple mechanisms, both immunologic, as exemplified by occupational asthma and extrinsic allergic alveolitis, and nonimmunologic. It is the nonimmunologically mediated, nonspecific airways obstruction from bronchial ~~irritation that is the topic of the present section.~~

Although the pathogenesis of the nonspecific airways obstruction associated with organic dusts has not been defined, it is apparent that there are numerous parallels between the airways disease resulting from these dust exposures and the lung disorders associated with exposure to cigarette smoke, which is also a complex mixture of particulates. This parallel has been best defined in individuals with grain dust exposure.

In this regard, the clinical presentation of grain workers with chronic pulmonary symptoms is indistinguishable from that found in cigarette smokers (Dosman et al., 1979). In addition, the falloff in values of pulmonary function (maximum midexpiratory flow rate) for age equivalent years of exposure for nonsmoking grain workers is about equal to that observed for nonexposed smokers (Dosman et al., 1979). Furthermore, the lung disease found in grain workers is clearly increased in severity in workers who also smoke (Becklake, 1980; Cotton & Dosman, 1978; dePico, 1979; dePico et al., 1977; Dosman et al., 1979; Warren & Manfreda, 1980).

Finally, nonspecific airways hyperreactivity in response to histamine is similar in cigarette smokers (Katila et al., 1981) and in some individuals with vegetable dust exposure (Jones et al., 1982). Thus, it is likely that the pathophysiologic changes occurring in response to cigarette smoke exposure can serve as a model for those which occur as a result of nonspecific

The effects of cigarette smoke which may serve as a prototype of the effects of organic dusts on the airways include: 1) inflammation; 2) increased mucus secretion; 3) increased airways permeability; and 4) nonspecific airways hyperreactivity.

Although the presence of an inflammatory process in the airways has not been evaluated in individuals with chronic exposure to these organic dusts, a number of observations suggest that such a process should occur in the lungs of these patients. In this regard, inhalation of a number of organic particulates results in an influx of inflammatory cells into the lung (Hunninghake et al., 1979; Hunninghake et al., 1980).

The mechanisms by which inflammatory cells are attracted to the lung by organic dust have not been defined. However, it is known that these dusts may contain endotoxin, an agent which is known to attract neutrophils to the lung following inhalation (Hunninghake et al., 1979).

In addition, it is also known that some of these dusts can activate the complement cascade and, thus, can generate complement derived chemotactic factors (Olenchok et al., 1978; Wirtz et al., 1984). These chemotactic factors are likely to attract inflammatory cells to the lung (Hunninghake et al., 1979). Finally, a number of inhaled particulates are known to stimulate alveolar macrophages to release a chemotactic factor for neutrophils (Hunninghake et al., 1980). This chemotactic factor may also attract neutrophils to the lung in these disorders. Thus, inhalation of organic dusts clearly has the potential by these or other mechanisms to trigger an inflammatory process in the airways.

In parallel with these observations, cigarette smokers also have large numbers of macrophages and neutrophils in the lung. These cells are detected pathologically, in the small airways and in the alveolar capillary membrane (Hogg et al., 1968). Increased numbers of these cells are also detected in ~~bronchoalveolar lavage fluid from these patients (Humminghake et al., 1979).~~

The presence of inflammatory cells in the airways of smokers is clearly associated with airways obstruction (Hogg et al., 1968).

Inhalation of these organic dusts is also associated, clinically, with increased sputum production (Dosman et al., 1979). Although the mechanisms which trigger increased mucus production in these individuals have not been defined, it is known that cigarette smoke can stimulate airway goblet cells to discharge their contents of mucus (Hulbert et al., 1981). In addition, prolonged cigarette smoking is associated with enlargement and increased numbers of these submucosal glands in the airways (Snider, 1981). It is possible that chronic inhalation of organic dust triggers increased sputum production in a similar manner. Irrespective of the mechanisms for increased sputum production, however, the presence of the mucus in the airways of these patients is likely to increase airways obstruction.

Normal airways' epithelium is quite impermeable to a variety of agents (Gerrard et al., 1980; Golden et al., 1978; Nadel, 1977). Cigarette smoke exposure has been shown to increase mucosal permeability in experimental animals (Boucher, 1980; Boucher et al., 1981). This increased mucosal permeability is thought to occur because of a disruption of the tight junctions or the airway epithelium (Jones et al., 1980). Increased mucosal permeability has also been demonstrated in smokers compared to nonsmokers. The increased mucosal permeability is usually associated with an inflammatory

response in the airways. It is thought that inflammatory cells increase mucosal permeability by one or both of the following mechanisms (Snider, 1981): 1) oxidant damage of the epithelium by free radicals derived from polymorphonuclear leukocytes; and 2) enzymatic cleavage of tight junctions by proteases released from inflammatory cells. Since inhalation of organic dusts is also associated with an inflammatory process in the airways, increased airway mucosal permeability may also be present in these individuals. This type of lesion also nonspecifically increases airflow obstruction in the airways.

It has recently been demonstrated that individuals with vegetable dust exposure have an increased nonspecific bronchial reactivity to histamine (Jones et al., 1982). The mechanism for this increased airways reactivity to histamine is unknown, however, it is known that the mucosal epithelium contains an abundance of nerve fibers that are sensitive to a wide variety of irritant stimuli. These irritant receptors are usually found close to the lumen and it has been demonstrated that damage to the tight junctions can increase the exposure of these nerve endings to agents present in the lumen (Golden et al., 1978; Nadel, 1977). Histamine is probably acting either by stimulation of these irritant receptors or a direct action on smooth muscle, both of which would be more accessible with increased permeability. Sellick and Widdicombe (1971) have demonstrated that cigarette smoke can also stimulate these receptors (Hogg, 1981). This type of stimulation leads to tachypnea, smooth muscle constriction and mucus hypersecretion (Boucher, 1980). Thus, exposure to vegetable dusts appears to result in an increased hyperreactivity in a manner similar to that caused by exposure to cigarette smoke.

To summarize: 1) Inhalation of vegetable dusts is associated with an increased frequency of symptoms of nonspecific airways obstruction; 2) there is reason to believe that the pathophysiology involved with these exposures is similar to that seen with inhalation of cigarette smoke; and 3) these dusts ~~probably act as nonspecific irritants which cause an inflammation in the~~ airways. This inflammation leads to increased permeability and bronchial hyperreactivity with consequent acute and chronic respiratory symptoms.

## 4.2 Etiological agents

### 4.2.1 Grain dust<sup>1</sup>

Grain harvesting, transportation, storage and processing is an essential industry in both developing and industrialized countries. World production of cereals was 1.69 billion metric tons in 1982 (UN, 1985). In the broad context of the trade, grain includes not only the edible starchy fruits of grasses but also the legumes and oil seeds. Grain is a staple in the diet of peoples throughout the world. When one considers the number of people employed in growing, harvesting, transporting, storing and processing grains, the potential population at risk to grain dust exposure worldwide must be measured in the tens of millions. For example, in the USA it is estimated that there are at least five million farmers and other agricultural workers exposed to grain dust in growing and harvesting grain, 225 000 workers in grain elevators and another 450 000 workers employed in flour, seed and other grain processing plants (Warren, 1982).

#### Components of grain dust exposure

The vegetable dust which comprises the bulk of grain dust arises from the pericarp surrounding the fruit, but also some starch, germ, leaf and stem material. With processing, heavier dust particles are lost leaving progressively more respirable particles. With milling, highly respirable flour is produced which poses a potential hazard for those subsequently exposed.

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<sup>1</sup>By Merchant, J.A. & Dosman, J.A.

prevent spoilage or loss from pests introduces yet another type of potential biological hazard for grain handlers. Chemicals commonly used in North America include the following fumigants: carbon disulfide ( $CS_2$ ), carbon tetrachloride ( $CCL_4$ ), malathion, aluminum phosphide ( $AlPO_3$ ), and methyl bromide ( $CH_3Br$ ). (Peters et al., 1982).

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#### Health effects arising from grain dust exposure

A variety of nonpulmonary and pulmonary disorders, many of them associated, arise from occupational exposure to grain dust (see Table 6). Conjunctivitis is common among those working in grain dust and appears to be related to dust level. (Broder et al., 1979) Dermatitis (grain itch) may occur in an epidemic fashion among those exposed to grain infested with the mite Pyemotes ventricosus. (Booth & Jones, 1952).

Grain fever is a fairly common complaint especially among new employees in dusty areas. (Broder et al., 1979; doPico et al., 1977) This condition resembles influenza and is characterized by fever, chills, headache, malaise, cough and sometimes chest tightness.

Table 6 Health Effects Associated with Handling Grain  
or Exposure to Grain Dust

Pulmonary disorders	Nonpulmonary disorders
Acute respiratory symptoms	Grain fever
Acute airflow obstruction	Dermatitis
Asthma	Conjunctivitis
Chronic bronchitis	Rhinitis
Chronic airflow obstruction	Mycotoxicosis
Pulmonary fibrosis	Chemical poisoning
Allergic alveolitis	

It appears to be the same syndrome as cardroom fever, a common complaint among those newly employed in dusty cotton mill cardrooms. Both of these conditions have been attributed to endotoxin exposure. (Neal et al., 1942; Pernis et al., 1961) The relationship between these acute febrile illnesses and subsequent respiratory disease is, however, unknown.

Occupational exposure to fumigants is common among North American grain handlers. Rankin in an unpublished report to NIOSH on the prevalence of chronic nonspecific lung disease among grain handlers, observed that over one half of the grain workers surveyed reported symptoms associated with such exposures. Peters and coworkers (1982) have recently associated exposure to carbon disulfide and possibly other fumigants with marked neuropsychiatric changes among several grain storage workers with long exposure to these chemicals. Again, adequate epidemiological evaluation of the prevalence and severity of such health effects among grain handlers has not been reported.

Rhinitis and asthma. Sensitization to a variety of constituents of grain dust may result in rhinitis and asthma in those exposed to grain dust. Such specific sensitization may be documented through skin testing, or if considered necessary, through inhalation challenge.

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Asthma which arises from grain dust exposures is indistinguishable from asthma arising from other exposures. Three patterns of asthma have been documented among grain handlers - the familiar immediate response which occurs within minutes and then tends to recover over one to two hours, a dual response with an immediate reaction followed by a more prolonged late response usually from four to eight hours after initial exposure, and recurrent asthma which may occur daily over many days. (Chan-Yeung et al., 1979; Davies et al., 1975; doPico et al., 1982; Warren et al., 1974)

Available evidence suggests that the prevalence of asthma among those with daily exposure to grain dust is quite low. (Cotton et al., 1983; Herxheimer, 1967) This is, no doubt, attributable to selection away from grain dust exposure by those adversely affected by rhinitis or asthma.

Chronic bronchitis. Chronic bronchitis, or chronic cough and phlegm, is perhaps the most common clinical manifestation of occupational exposure to grain dust. Wheezing and chest tightness are also common complaints with shortness of breath somewhat less commonly reported. Chronic bronchitis is generally reported to occur in between 10% and 50% of grain handlers depending on the concentration and duration of grain dust exposure and the extent of cigarette smoking among the population under study (Becklake, 1980; Warren, 1982). Grain dust and smoking appear to be additive as risk factors in

chronic bronchitis (Cotton et al., 1983; Dosman et al., 1980). Symptoms of chronic bronchitis are also associated with a decreased level of lung function in a very high proportion of grain handlers with objective evidence of airways obstructions, reporting chronic cough and phlegm (Siemens et al., 1980). Although it is generally recognized that chronic bronchitis is associated with dust concentration, good dose-response studies relating respirable dust to respiratory symptoms or function are not to be found in the literature.

Airways obstruction. Apart from episodes of asthma which occur in some individuals exposed to grain dust and which may result in significant declines in expiratory flow ( 20%), small, but statistically significant declines in FEV<sub>1</sub> and other expiratory flow rates have been found among grain handlers. (McCarthy et al., 1985). These decrements in lung function appear to be similar in magnitude to those experienced by workers exposed to cotton, flax and hemp dusts. These declines continue across the workshift and tend to reverse prior to the next shift or over a week-end. Whether such acute declines are associated with progression to irreversible airways obstruction is unclear and awaits prospective evaluation (Warren, 1982). Similarly, the relationship between these shift declines and respirable dust levels have not been adequately studied.

There is cross-sectional evidence that chronic and irreversible airways obstruction results from prolonged occupational exposure to grain dust (Warren, 1982; Cotton et al., 1983). The few prospective evaluations would appear to support this view, although these studies are short in duration and do not involve large numbers of subjects (Becklake et al., 1980; Broder et al., 1980). Physiologically, changes in lung functions are similar to

those arising from exposure to cigarette smoke (Cotton et al., 1983). Several studies have suggested that both cigarette smoking and grain dust are significant risk factors associated with airways obstruction among grain handlers (Becklake et al., 1980; Cotton et al., 1983).

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Cotton and colleagues (1983) recently completed a very well controlled study of Saskatchewan grain elevator workers in which they matched smoking and nonsmoking grain workers with smoking and nonsmoking community controls. Both smoking and grain dust exposure were found to be associated with decreased lung function with smoking being somewhat more prominent. Generally these effects were additive except among those exposed to grain dust for less than five years, where there was evidence of an interaction affecting measures of peripheral airway function. Evidence of worker selection out of this industry was noted by the authors and may well explain these quantitative differences between exposure duration categories.

Interstitial lung disease. Although pulmonary fibrosis attributed to silica exposure has been reported to occur among dockers handling grain, evidence supporting this finding is weak (Dunnes et al., 1946). Documented cases of hypersensitivity pneumonitis have been observed among workers exposed to grain contaminated with Aspergillus fumigatus and Aspergillus flavus (Patterson et al., 1974; Yocum et al., 1976). Malt workers in Scotland have also been studied and a prevalence of hypersensitivity pneumonitis of 5.2% associated with Aspergillus clavatus has been reported (Blackadder, 1980). Except among those routinely exposed to moldy grain, the occurrence of hypersensitivity pneumonitis is rare.

#### 4.2.2 Jute and Hard Hemps<sup>1</sup>

Dusts from these fibers, on present knowledge, are included in the group which causes bronchial irritation and non-specific airways obstruction.

##### Jute and related fibers

Sources of material. Jute is a bast fiber obtained from the inner bast tissue of the bark of two herbaceous annual plants, Corchorus capsularis and Corchorus oblitarius, which belong to the family Tiliaceae. Since ancient times jute has been cultivated in India as a fiber-producing plant for making clothing and cordage. Its main use in present times is for making sacks and bags, carpet yarns, and cloth backings for linoleum and carpet. It is increasingly threatened by other bast fibers and synthetic materials and by new methods of packing and transportation which do away with the use of sacks and bags.

Bangladesh and India grow 90% of world supplies. The rest comes mainly from Burma, China and Thailand. Grown during the rainy season, jute thrives in damp heat and is harvested three to five months after sowing when it has reached a height of one meter. Plants are cut with a sickle close to the ground; in flooded areas the cutters have to dive under water to cut the stems.

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<sup>1</sup>By Schilling, R.S.F.

The jute fibers are loosened from the bark by retting, which is induced by chemical or bacterial methods. It is washed and dried, tied in bundles ready for conversion into yarn. At an early stage after retting the jute fiber has to be separated from the bark by hand batting or mechanical ~~beating. This is usually done in the producing country. Jute is graded and~~ packed into bales. Grading depends on various fiber characteristics such as length, fineness, and strength. Fibers that can be spun into fine yarns are the most valuable (Anonymous, 1981).

Bales of fibers are opened and blended in the manufacturing countries. Oil, water, and emulsifiers are added to soften the jute, which is spread into a sliver ready for carding. The carding draws out the fibers into parallel lines and the remaining processes of further drawing, roving and spinning are similar to those used for other textile fibers.

Sunn hemp (Crotalaria juncea), which closely resembles true hemp, is a member of the pea family (Leguminosae). It is grown in India, mainly for its fibers, but it is also used as a manure. It is lighter and stronger than jute and is used for ropes and bags. The fibers are retted and processed by the same methods that are used for jute.

Kenaf is a bast fiber obtained from the stem of Hibiscus cannabinus. It closely resembles jute, is similarly processed, and may be blended with it. Like the other bast fibers, roselle and urena, kenaf belongs to the mallow family (Malvaceae) which has become one of the most important of all fiber plant families. It is adaptable to various kinds of soil and climatic conditions, but is sensitive to frost, so that its cultivation is limited to tropical and subtropical regions.

Characteristics of jute. Unlike cotton, there have been very few reports published on the characteristics of jute dusts. An investigation in a jute mill in Scotland revealed total dust concentrations of  $5.5 \text{ mg/m}^3$ , consisting of minerals (46%), cellulose (45%), and plant debris (9%). The respirable dust concentrations were comparatively low at  $0.3 \text{ mg/m}^3$  (Mair et al., 1960). In an English jute mill total dust concentration ranged from 2.7 to  $3.6 \text{ mg/m}^3$ . Respirable dust concentrations ranged from 0.02 to  $0.2 \text{ mg/m}^3$ . The percentage of protein in the jute dust was about 10%, that is about half the typical values for cotton dust (Gilson et al., 1962).

The available information on the characteristics of dust is limited. Nevertheless, it can be concluded that jute mills usually have higher dust concentrations than mills processing hard hems. Both hard hemp and jute dust, like cotton dust, consist of heterogeneous materials, which include broken fibers, plant debris, earthy materials, dead and living microorganisms and their products. Judged by the response of exposed workers, jute and hard hemp dusts do not appear to contain the agent or agents causing byssinosis in sufficient quantities to produce the characteristic symptoms of chest tightness on the first day of the working week.

To summarize, the available evidence suggests that the dusts produced by the processing of these fibers present a relatively minor health hazard, compared with cotton or flax or soft hemp. This is because throughout the world they are used in much smaller quantities and are relatively less toxic.

Sources of exposure. In producing countries, little is known about sources and levels of dust exposure. Dust exposures should be negligible in both harvesting and in retting. In the preparation and production of fibers for spinning there is heavy dust exposure in the early processes of opening, ~~batching and carding. Dust concentrations are much lower in the later~~ processes of spinning (Gilson et al., 1962). Unlike flax (El Batawi & Hussein, 1964) no studies have been reported of nonoccupational exposure to jute and hard hemp dusts by members of the family from preparing fibers in the home.

Clinical findings. Arlidge (1892) and Wilson (1902) first reported that jute dust caused respiratory disease. Reports over the last two decades indicate that exposures to elevated concentrations of this dust cause persistent cough and phlegm, with a fall in ventilatory capacity during a work shift. However, there is no evidence that the mechanism responsible for these effects is synonymous to that causing byssinosis which is thought to be pharmacologically based.

Epidemiological findings. The first attempt to identify byssinosis was in 1956, using the special questionnaire on respiratory symptoms approved by the British Medical Research Council Committee on Research into Chronic Bronchitites which was reproduced as Annex 1, pp. 72-76, in a WHO Technical Report No. 684 (WHO, 1983). Forty-six Dundee workers who had been employed in dusty sections of a jute mill for many years, were interviewed. None were found to have the characteristic symptoms of byssinosis (Schilling, 1956). This negative finding has since been repeated by Mair and others (Mair et al., 1960; Gilson et al., 1962; Gandevia & Milne, 1965; Siddhu et al., 1966; Noweir et al., 1981).

However, these studies show that jute workers do have nonspecific symptoms of respiratory irritation which are related to dust exposure. These symptoms are unlike those of occupational asthma. In the Yugoslavian study of 91 nonsmoking jute workers aged between 17 and 41 years, the prevalence of persistent cough was 9.8% and persistent phlegm 13.2% (Valić & Zuškin, 1971).

There have been four investigations of the acute effects of jute dust on respiratory function. Mair and colleagues (1960) found no significant fall in forced expiratory volume ( $FEV_{0.75}$ ) during the shift. There was a similar negative result in another group of jute workers (Gilson *et al.*, 1962). In nine workers in less dusty jobs and in eleven workers in dustier jobs, there was no obvious acute effect in either group on ventilatory capacity ( $FEV_{0.75}$ ) during the shift.

Gandevia and Milne (1965) measured ventilatory capacity ( $FEV_1$ ) in 46 men exposed to jute dust, while making felt and wadding. There was a significant, confined mean decrease in  $FEV_1$  on the first day at work. The decrease was largely attributable to those who smoked. Men with productive cough, who were mostly smokers, had a highly significant reduction in  $FEV_1$  on the first shift of the week. While there was no definite evidence that acute loss of ventilatory capacity was related to degree of dust exposure, the authors suggested that subjects with a productive cough may have a greater tendency to react to inhaled irritants.

Valić and Zuškin (1971) measured ventilatory capacity over the first work shift of the week in 91 jute workers. The tests used were  $FEV_1$ , forced vital capacity (FVC) and peak expiratory flow (PEF). Similar tests were made

for 60 cotton workers. All the subjects were female nonsmokers. The jute workers had significant reductions in all three lung function measurements over the work shift, but the reductions were less than those of the cotton workers (Table 7).

Table 7. Mean FEV<sub>1</sub>, FVC, and PEF Changes in Cotton and Jute Workers over a Work Shift.

Group	N	FEV <sub>1</sub>			FVC			PEF		
		ml	%	P	ml	%	P	l/min	%	P
Cotton	60	-138	-4.1	0.01	-108	-2.7	0.01	-23	-5.1	0.01
Jute	91	-121	-3.8	0.01	-57	-1.5	0.01	-15	-3.5	0.01

(Source: Valić and Zuškin, 1971)

No studies have been reported on the chronic effects of jute dust on lung function. Radiological examination of Dundee jute workers was undertaken by Mair and colleagues (1960). Lateral and posteroanterior films were taken and developed under standard conditions. They were read by seven observers who found no evidence of radiological changes that could be related to exposure to jute dust.

There have been no immunological studies of subjects exposed to jute dust, apart from the investigation by Popa and coworkers (1969) of sensitization to cotton, hemp, flax and jute antigens. Immediate skin reactions were rare. Delayed reactions were often present. The incidence of positive reactions was similar in subjects with and without byssinosis. They found several antibodies against textile dust antigens in the serum of

workers. These probably had no pathogenic significance. Inhalation tests were negative in all the 34 textile workers exposed to hemp, flax and jute, except for the three who had byssinosis grade II. This study was made on subjects exposed to a mixed textile dust. This makes it difficult to draw any conclusions about the antigenic properties of jute.

Maximum permissible levels. Information on which to base permissible dust levels for jute and hard hems is sparse. As they are known to be irritant, they should be controlled to a level below that recommended for inert dusts. A tentative figure of  $2 \text{ mg/m}^3$  total dust has been suggested. It is based on the survey in the Naval Dockyard ropery (Munt et al., 1965).

Research priorities. Little is known about the chronic effects on the respiratory tract of exposure to jute dusts. No cross-sectional or longitudinal studies which include lung function have been made of populations at risk for evidence of permanent respiratory impairment. The mechanisms by which these dusts give rise to acute and chronic effects are unknown. More information is needed about the adverse health effect of exposure to dusts from bast fibers, such as kenaf, which belong to the mallow family. They have become an important source of material for cordage. The information on which to base permissible exposure levels for jute dusts is inadequate. Vegetable dust emitted from processing bast fibers should not be dismissed as a nuisance dust, without fuller investigation of its health effects on people at work.

#### Hard hems and related fibres

Sources of material. Hard hems are derived from the leaves of certain plants. The fibers are used for making cordage, but are too hard or stiff for

most fabrics. Two of the most important cordage fibers are abaca or Manila and sisal. Sisal is known to give rise to dust causing byssinosis.

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Abaca, or Manila hemp is obtained from the plant, Musa textilis, which belongs to the banana family (Musaceae). It is grown mainly in the Phillipines, but during the Second World War, it was introduced into India, Indonesia and Central America. Leaves grow to a height of about 2.5 m before harvesting. The fibers are removed from the leaf sheaf by a stripping process. They are then dried, cleaned and baled, and readied for processing, which is similar to that used for making other vegetable fibers into ropes and twines.

Other leaf fiber plants of commercial value belong to the Agave family. They include Fureraea gigantea, which produces Mauritius hemp and Phormium tenax, which produces New Zealand or St Helena hemp.

Characteristics of dust. As was true for jute fibers, the literature is essentially devoid of data characterizing the hard hemp dusts. In an English rope factory, using St Helena hard hemp, dust concentrations in opening, spreading and scutching departments had a mean value of  $2.1 \text{ mg/m}^3$  total dust. They were negligible in spinning departments and in the rope walk. In the early processes, respirable dust concentrations were as high as  $1.5 \text{ mg/m}^3$  (Munt et al., 1965). In another English rope factory using sisal, Manila and St. Helena hems dust concentrations were relatively low, with respirable dust levels generally less than  $0.5 \text{ mg/m}^3$  (McKerrow et al., 1965).

Sources of exposure. In producing countries, little is known about sources and levels of dust exposure. Dust exposures should be negligible in both harvesting and in retting. In the preparation and production of fibers for spinning, there is heavy dust exposure in the early processes of opening, batching and carding. Dust concentrations are much lower in the later processes of spinning (Gilson et al., 1962). Unlike flax (El Batawi & Hussein, 1964) no studies have been reported of non-occupational exposure to jute and hard hemp dusts by members of the family from preparing fibers in the home.

Clinical findings. The first evidence that exposure to hard hemp dust could give rise to respiratory symptoms came from population studies undertaken in the last 20 years. These studies show that exposures to high dust concentrations cause persistent cough and phlegm, with a fall in ventilatory capacity during a work shift. As is true with jute dusts, there is no evidence that exposure to hemp dust causes byssinosis. The observed effects of exposure are probably mechanical rather than pharmacological in origin and are caused by a rapid reflex response, producing bronchoconstriction. Therefore, the mechanism of response to this dust is distinct from that causing byssinosis.

Epidemiological findings. A woman employed in a rope factory using Manila hemp, St. Helena hemp, and sisal, was admitted to the hospital with a history which suggested that she might have byssinosis. Several of her companion workers were similarly affected with respiratory symptoms suggestive of byssinosis. A study was made of the small population of 42 workers at risk. Excluding those who worked with sisal (in a separate location), none gave a history of byssinosis, but in the dustiest section a few

chronic cough and sputum. The dust exposures were relatively low, the highest being  $1.1 \text{ mg/m}^3$  total dust and  $0.47 \text{ mg/m}^3$  respirable dust in the preparation room.

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~~A similar study was undertaken in another rope factory in a Royal Naval Dockyard. It also handled Manila and St Helena hemsps and sisal. Dust concentrations were higher than those in the first factory, ranging from 0.11 to  $4.51 \text{ mg/m}^3$  total dust and 0.02 to  $1.46 \text{ mg/m}^3$  respirable dust. The highest concentrations were in the preparing room. None of the 82 workers examined gave a history of byssinosis, but 9 (22%) of those working in the preparing room gave a history of chest tightness associated with their work. This proportion was significantly higher than those found in women working in other parts of the dockyard. None of the men, who generally worked in less dusty jobs in the ropery, had this complaint.~~

Lung function tests were made of the workers in both these rope factories. In the factory with the lower dust exposures, significant falls during the work shift were found in the mean value of  $FEV_1$  and FVC. The falls in ventilatory capacity were not greater in those with symptoms of chronic cough and sputum than in those without these symptoms.

In the second rope factory similar acute losses of  $FEV_1$  were recorded among the women workers, but not among the men in the rope walk, where dust exposures were low (mean level:  $0.5 \text{ mg/m}^3$  total dust). In this factory a random sample of 41 women from other parts of the dockyard, matched for age with the rope workers, were examined. There was no evidence that the rope workers had suffered any permanent impairment of  $FEV_1$  after adjusting for

age, height, and smoking habits. The numbers, however, are too small to draw any conclusions as to whether or not hard hemp dusts cause permanent respiratory impairment.

No reports have been found of investigations of radiographic changes or of immunological studies of subjects exposed to hard hemp dust.

Maximum permissible levels. Information on which to base permissible levels for jute and hard hems is sparse. As they are known to be irritant, they should be controlled to a level below that recommended for inert dusts. A tentative figure of  $2 \text{ mg/m}^3$  total dust has been suggested. It is based on the survey in the Naval Dockyard ropery (Munt et al., 1965).

Research priorities. Little is known about the chronic effects on the respiratory tract of exposure to jute dusts. No cross-sectional or longitudinal studies which include lung function have been made of populations at risk for evidence of permanent respiratory impairment.

The mechanisms by which these dusts give rise to acute and chronic effects are unknown. The information on which to base permissible exposure levels for hard hemp dust is inadequate. However, using limited data, a tentative figure of  $2 \text{ mg/m}^3$  total dust has been recommended for hard hems.

Vegetable dust emitted from processing leaf fibers should not be dismissed as a nuisance dust, without fuller investigation of its health effects on people at work.

4.2.3 Kapok, Coir, Tea, Coffee, Chili, Cocoa, and Cinnamon<sup>1</sup>4.2.3.1 Kapok

~~Source and uses. Kapok is the fiber obtained from the fruits of the~~  
Ceiba pentandra tree. It grows in tropical countries such as India, Indonesia, the Philippines, Sri Lanka, Thailand and in East and West Africa. The tree grows up to 30 m in height. The fruits are spindle-shaped pods about 15 cm in length and 5 cm in diameter at the center. The green pods turn black upon ripening. When the outer husk is removed, balls of fiber, each arranged around a central pepper-like seed, are exposed. These fluffy balls are disposed around a central fibrinous core. Each fiber measures 8 to 30 mm in length, the average being 19 mm.

Kapok fiber is similar to cotton in appearance, but is yellowish rather than white and has a sheen. The fiber is unsuitable for spinning into textiles: it is weaker than cotton and too smooth and slippery, being only a sixth of the weight of cotton. It repels water (probably due to a waxy cutinous covering) and does not lose its buoyancy even when left in water for weeks. These qualities make kapok suitable for use in life saving equipment such as life belts and life jackets (Kirby, 1963).

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<sup>1</sup>By Uragoda, C.G.

Kapok is widely used for stuffing pillows, mattresses and cushions. One of its main advantages is its resistance to pests. It has a low thermal conductivity and hence is used for insulation. It is one of the best sound absorbers available per unit weight and is used for this purpose in aircraft where its lightness is an added advantage. It is widely used in all the producing countries and the surplus is exported. The largest exporter is Thailand, followed by Indonesia. Most of the industrialized countries import the fiber, the leading buyers being France, the Federal Republic of Germany, the Netherlands and USA.

Sources of exposure. The fruits mature at different times and therefore the harvesting is spread over many months. Dry pods are husked manually when the fluffy balls are exposed. Extraction of the fiber by removing it from the seed and the core is done either manually or mechanically.

Electrically powered machines are usually capable of ginning between 275 and 550 kg of kapok a day. The machine is essentially a cylindrical cage made of metal sheet or wire mesh with a rotary axis running vertically in the center. The axis has a pair of horizontal metal rods attached to it at the bottom which breaks up the kapok fiber from the seed. The fluff is propelled upwards by a series of fan blades attached to the axis at several points above the level of the rods. The fluff escapes from the machine via a wide duct at the top of the cage and settles in a separate enclosed room. The seeds and cores are removed from the machine at intervals. The cores to which some fibers are invariably attached are stored in bags for subsequent reginning once the kapok season is over. This process is more dusty than the initial ginning. The ginned kapok is mechanically compressed into rectangular bales, wrapped in jute cloth and fastened in hoop iron prior to export.

Each ginnery employs 6-15 workers who are expected to perform any type of work connected with ginning: feeding the machine with kapok pods; collecting and bagging cleaned kapok; sifting the seeds from the cores; and bagging and storing them. All the workers are therefore equally exposed to kapok dust

~~(Uragoda, 1977). The ginneries are badly ventilated and there is no special~~

provision for dust suppression. The workers are, as a result, exposed to much dust. Those who husk the pods in the producing areas and those who handle the fiber in various industrial processes in both the producing and importing countries are, however, exposed to the dust to a lesser degree.

Clinical and epidemiological findings. In the only available study on the health of kapok workers, 6 men and 35 women in five ginneries in Colombo were investigated (Uragoda, 1977). Their average age was 34.5 years and their average period of service in the kapok industry 10.7 years. Fourteen workers had over ten years of service. The following findings are based on this study.

Mill fever. Mill fever, which is a trivial, self-limiting illness characterized by sore eyes, sneezing, mild pyrexia, muscular pains, cough or headache on initial exposure to dust, is quite common in the kapok industry. It occurred in 28 (78%) of the 36 workers who were able to give a history. Mill fever also occurs in new workers who are exposed to other vegetable dusts such as cotton, hemp, flax, jute and grain. Among kapok workers the most common symptoms were in relation to the eyes: nearly 50% of the workers had irritation, redness or lacrimation. Mill fever symptoms in kapok workers abated in one to 14 days (average four days). It hardly required treatment other than aspirin. It was of no economic importance to the industry as none of the kapok workers lost any working days as a result of it.

Chronic bronchitis: - Chronic bronchitis, which is an uncommon condition in Sri Lanka, occurred in seven (17%). Six were non-smoking women, therefore, the condition was not related to smoking. Three of these seven workers with chronic bronchitis had over ten years service in the industry.

Byssinosis: - While byssinosis occurs in workers handling other vegetable fibers such as cotton, flax and soft hemp, it has not been reported in kapok workers in spite of the similarities between cotton and kapok. None of the workers admitted to the study had evidence of byssinosis, nor did they exhibit significant radiological changes (except for three who had evidence of healed tuberculosis).

Skin testing with kapok antigen proved negative in all 21 workers tested. Fourteen samples of sera on which precipitin tests were carried out did not show any reactions to extracts of kapok. Seven samples reacted to Micropolyspora faeni antigen but none of them had evidence of farmer's lung.

There is no information available on lung function tests, lung pathology, environmental exposure data or dose response relationships.

#### 4.2.3.2 Coir

Source and uses. Coir is the fiber of the husk of the matured coconut. The coconut palm, Cocos nucifera, grows extensively in tropical islands and coastal areas such as the Kerala State in India, Indonesia, Madagascar, the Philippines, Seychelles, Sri Lanka, the South Sea Islands, tropical Africa and tropical America. The world production of coir is in the region of a quarter

of a million tonnes per year. India produces about half this amount but it is mainly used locally. One hundred thousand tonnes enter the world markets and Sri Lanka exports 90-95% of this amount. Other countries such as the Kenya, Malaysia, Mexico, the Philippines, Seychelles, Thailand, Trinidad and the ~~United Republic of Tanzania account for small quantities.~~

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Coir is imported by many industrialized countries, the main consumers being Australia, Federal Republic of Germany, Italy, Japan, South Africa and the United Kingdom (Subasinghe, 1973).

Coir has many uses. The thick long variety or bristle fiber is used in the manufacture of brushes. Mattresses are made mainly out of the short thin variety. A recent development has been the impregnation of coir with rubber for mattresses and upholstery such as car seats. Coir rope stretches considerably without breaking. It is resistant to sea water and hence was used by early voyagers for cables and riggings. White fiber is sometimes used in the manufacture of oil filters. Coir is also used in the production of nets, twine, sacks, matting and brooms (Subasinghe, 1973).

Characteristics of the dust. The coconut consists of the outer husk and the large central seed. The husk which is the mesocarp of the fruit consists of a collection of fibers bound together by a light pith. Pith, a brown spongy substance similar to cork, is the source of the dust in the coir industry. The particle size of the dust varies from very small to large; the latter can measure 3 to 4 mm in diameter. The chemical composition of coir dust is similar to that of sisal; consisting of cellulose, lignin, ash and pentosans. Sisal contains a higher proportion of cellulose and pentosans.

Sources of exposure. The green outer surface of the husk becomes brown upon ripening. The fiber from green husks is white and is more in demand than the brown variety from the ripe fruits, but only a small quantity of it is produced as this is mainly a cottage industry. The manufacture of copra, dessicated coconut and oil are large industries which utilize the dried brown nut; therefore, the output of brown fiber is large.

Retting or soaking the husks in water is required to facilitate the separation of fiber from the pith. The period of retting is as long as six to nine months in the case of green husks but only one month for brown husks. If the husks are crushed mechanically, they need only a few minutes of soaking, but the dust content is high in the fiber that is produced.

In Sri Lanka, while some fiber is extracted as a cottage industry, most of the production is done in mills which number nearly 600 and have an estimated labor force of 40 000 to 50 000. The majority of these mills are semi-mechanized where a worker has to hold a retted husk against a rapidly rotating drum fitted with a number of vertical nails. The other end of the husk is similarly treated. The process is repeated twice or thrice on a second drum with more closely fitted nails. This maneuver removes most of the pith which, together with the short fibers, falls to the ground leaving a hank of long fibers in the worker's hand. In a fully mechanized process, after a few minutes soaking, the husks are fed into a decorticator where they are crushed and beaten by metal rods, and the pith liberated. The fiber is then sifted to remove any loose pith, washed and dried, usually in the sun.

Following this treatment fiber is transported to central factories for processing before export. This processing consists of bleaching to improve the color and quality, removing the remaining pith, separating the fiber into different grades such as mattress and bristle fiber (in order to conform to ~~the requirements of importing firms abroad) and compressing the fiber to~~ conserve shipping space (Uragoda, 1975).

Bleaching is done in separate chambers using sulfur dioxide as the bleaching agent. Coir is stacked on a wooden trellis raised 20 cm from the floor of the chamber. A bucketful of burning sulfur is introduced underneath so that the fumes of sulfur dioxide percolate upwards through the fiber. The fumes finally escape through a vent between the roof and the top of the wall in the chamber. However, the workers are exposed to sulfur dioxide (Uragoda, 1981) which, being a heavy gas, tends to drift downwards towards the ground.

The fiber meant for mattress and upholstery work is teased in a machine with a rotating spiked drum. This fiber, for shipping convenience, is then spun into rope-like cords which are wound into tight coils weighing 50 kg. These cords are untwisted in the importing countries. Bristle fiber which is thicker and longer, is cleaned by hackling through a steel comb. This work is done by teams of women who work at long benches fitted with these combs.

Much dust is generated during separation of fiber from the pith and also in the various processes preparatory to export. None of the workers wear masks, and there is no special provision for ventilation in the mills and factories. Teasing and twisting are two of the most dusty processes and in large factories, ducts fitted to the machines carry the dust to a central point where it is collected in sacks.

Most of the dust is extracted from the exported fiber but workers handling these bales of coir in the importing countries are exposed to some dust residue.

Clinical and epidemiological findings. The only available study on the possible effects of coir dust is from Sri Lanka (Uragoda, 1975). These findings should be valid for the whole industry since Sri Lanka contributes 90% to 95% of the world trade in coir. Seven hundred seventy-nine workers (684 men and 95 women) in two coir processing factories in Colombo were clinically and radiographically examined. Their average age was 30.1 years and average period of service, 11.2 years; 67.6% had worked for more than five years, and 30.3% for more than 14 years.

Respiratory symptoms occurred in 20 (2.6%) of the 779 workers: cough (17 workers), expectoration (10), dyspnea (10), wheezing (6), chest pain (1) and hemoptysis (1). There were 22 workers with radiographic lesions: small rounded opacities (6 cases), small irregular opacities (2), opacities suggestive of active tuberculosis (1) and inactive tuberculosis (10), large opacities (2), emphysema (2) and cavity (1). There was no radiographic deterioration in these workers when examined five to ten months later. In a control group of 591 age matched workers from an engineering firm there were 23 with abnormal radiographs. This difference was not statistically significant and suggested that coir workers did not develop radiographic lesions due to their occupation.

Furthermore, this study found no increased susceptibility to asthma, chronic bronchitis or tuberculosis: their incidence was no higher than for the general population. There were six cases of asthma, three of chronic

bronchitis and nine with definite evidence of past or present tuberculosis. There was no evidence of byssinosis in any of the workers.

Sixteen workers who were engaged in bleaching of coir were studied (Uragoda, 1981). ~~Their average age and period of service were 34.3 and 11.3~~ years respectively. None of them showed evidence of chronic bronchitis, but three had past or present evidence of tuberculosis. This prevalence rate was higher than for the general population, but the number was too small to conclude that the disease was more common among them. All 16 workers had stomatological problems, namely dental caries (13 cases) and recession of gums (13). Sulfur dioxide dissolves on the moist surfaces of teeth and gums; thus, the resultant sulfurous and sulfuric acids were probably responsible for these lesions.

#### 4.2.3.3 Tea

Source and uses. Tea is manufactured from the young leaves and tender tips of the plant Camellia thea. It is grown extensively in Bangladesh, China, India, Indonesia, Japan, Kenya, Papua New Guinea, Sri Lanka and Tanzania. If allowed to grow uninhibitedly the tea plant develops into a tree, but regular pruning, as is done in commercial cultivation, restricts it to a shrub. The plant grows best on elevated land. A large tea plantation or estate has its own factory for the manufacture of tea.

The tender leaves and tips are plucked by women, usually every 8-10 days, and brought to the factory where these are withered by blowing warm air over them. The withered leaves are then fed into a series of rollers which break them up into small pieces. These bruised leaves are spread on trays and

allowed to ferment and then passed through a drier at which point they become the familiar black tea. Finally the black tea is sifted in mechanical sifters into different sizes and packed in plywood boxes, each containing 40-50 kg in weight. The bulk tea in plywood boxes is then transported to cities for local distribution or export. During sifting and packing a fine dust known as tea fluff is liberated. Exhaust fans, which are usually fitted into the sifting and packing areas of the factories, are only partially successful in removing this fluff, and the workers involved in these processes are covered with this golden coloured dust at the end of the day's work.

The manufacture of green tea is different. The tender leaves and tips are first steamed in a revolving cylinder and afterwards rolled and dried. The processes of withering and fermentation are omitted. Green tea is used mainly in China and Japan. There is a small market for it in other countries such as the USA. On the other hand, black tea is drunk in almost all the countries of the world, the principal users being Australia, South Africa, United Kingdom, USA, the Middle East and Europe.

The flavor of brewed tea depends on the tea itself as well as the quality of the water used. Different countries prefer different blends of tea. Each estate's tea has its own distinctive quality, and very often several grades of tea have to be blended in order to obtain a product which satisfy the requirements of the importing countries. A category of highly specialized personnel known as tea tasters provide formulas delineating proportions in which teas selected by them should be mixed. In deriving the formulas, they consider particle size, flavor, and color of the tea. Large export firms handle the work of blending which is done either manually or mechanically.

Mechanical blending is relatively dust-free but the mixing blades can break up the tea into smaller particles. Manual blending is free of this disadvantage and is preferred when buyers stipulate a large particle size. The bulk tea that is brought from tea estates to these exporting firms contain some ~~residual fluff and during manual blending, large quantities of this dust are~~ discharged into the atmosphere -- exposing workers to high dust concentrations.

Sri Lanka is the world's largest exporter of tea, with India and Kenya coming next in order. Importing firms in some of the large tea consuming countries such as the United Kingdom may blend the teas again. It is then packed for distribution. These processes are largely done mechanically, and the workers are not exposed to as much of the fluff (which in any case would have been reduced in quantity during sifting, packing and then blending in the producing countries). Though millions of workers are involved in tea production throughout the world, only a small proportion of them -- tea factory workers and blenders -- are subject to heavy exposure.

Clinical and epidemiological findings. Castellani and Chalmers (1919) working in Sri Lanka were the first to describe an occupational lung disease among tea workers. They described two related conditions which they named tea factory cough and tea taster's disease. The former affected workers in tea factories who suffered from loss of weight, fatigue, and cough with mucopurulent expectoration. Tea tasters, whose duty was to judge the quality of tea, had similar symptoms which were attributed to the inhalation of microorganisms upon sniffing tea leaves.

More recently a case of asthma in a man who supervised the manufacture of tea in a factory was reported from Sri Lanka (Uragoda, 1970). He developed an attack of asthma within a few minutes of entering the sifting or packing rooms where the atmosphere was laden with tea fluff. Provocative inhalation of tea fluff in this man triggered an attack of asthma in five minutes. A radiograph of the chest was normal. A positive reaction of the immediate type was obtained on skin testing with tea fluff antigen.

Ebihara (1975) described two patients in Japan who were considered to have allergic symptoms of headache, cough, expectoration, stridor, dyspnea and rhinitis which he thought were caused by airborne cilia from tea leaves. Grandjean and coworkers (1979) described the spirometric findings in 61 women and 9 men who worked in two tea packing plants in France. There was a fall in FEV<sub>1</sub>. They concluded obstructive impairment was due to a mechanism involving irritation rather than a tea allergy.

A survey of 125 workers (108 men and 17 women) who blended tea in a firm in Sri Lanka showed that 36% had respiratory symptoms (Uragoda, 1980). Their average age was 44.1 years and their average period of service in the tea blending industry was 22.9 years; 83.2% had worked in the industry for over 20 years. Chronic bronchitis was diagnosed in 31 (24.8%) workers and asthma in 8 (6.4%). The incidence of these two diseases in tea workers was higher than in the general population. It was found that the incidence of tuberculosis was no higher than in the general population. Radiography of the chest was normal. Lung function tests were not done.

A similar high incidence of asthmatic and bronchitic symptoms was reported in a tea bagging plant in the USA (Castellan, 1980). The presence of chronic cough and chronic bronchitis in relation to the manufacture of herbal tea in the USA has also been reported (Castellan et al., 1981). This tea was ~~prepared from nearly 70 ingredients of which black tea was one.~~ An unexpectedly high prevalence of respiratory symptoms occurred on the first working day of the week, but this was not supported by lung function tests.

#### 4.2.3.4 Coffee

Source and uses. Coffee, along with tea, is a universal beverage. It is obtained from the berry of the coffee plant which grows extensively in tropical regions. The world's largest producer of coffee is Brazil which accounts for 40-70% of the world output. Other countries of tropical America, tropical Africa, the Middle East, South East Asia and the Pacific Islands share most of the remaining market.

There are several species of coffee but the most extensively grown is Coffea arabica, while other important varieties are C. canephora and C. liberica. The size of the berry and the flavor vary in the different species. Each berry has two central seeds or beans which constitute the green commercial coffee.

Harvesting is spread over several months, the seasons varying from country to country. The ripe berries which have ideally attained the deep cherry red color are picked, brought to the factories and processed to produce the green coffee. Picking methods vary but it is always a labor intensive procedure and involves the majority of the workers engaged in coffee

Coffee seeds are extracted from the berries in most countries by a dry method, i.e., they are dried in the sun until fermentation occurs. The resultant outer coverings of the fruit are then crushed by various methods and the seeds separated off. Fermentation imparts the correct flavor to the coffee. Availability of sufficient water is a factor in the wet method practiced in some regions such as the West Indies. The fresh berries are crushed, the seeds with a slimy coat are separated from the pulp, allowed to ferment, washed and then dried. In both procedures residual dust and chaff remain with the seeds. The green coffee is then packed in sacks and exported.

Coffee has to be roasted and then ground or powdered before consumption and this is done in factories in the consuming countries. Heavy exposure to coffee dust takes place when the sacks of coffee are emptied, before roasting which is usually done in revolving cylinders heated to over 200°C. Workers who handle green coffee in both the exporting and importing countries are also exposed to coffee dust and chaff.

Since coffee production is a widespread industry, large numbers of workers throughout the world both in the producing and consuming countries are exposed to this dust. In the USA alone it was estimated that in 1970, 9000 workers were engaged in roasting and grinding coffee in 335 factories which handled over a million tonnes of green coffee (Bernton, 1973).

Clinical and epidemiological findings. There is extensive information in the world literature on the effects of coffee dust on workers. Kaye and Freedman (1961) found that nearly 10% of the 400 workers engaged in a coffee manufacturing plant in Canada had allergic symptoms. They concluded that the

allergen was in the raw coffee and the chaff and that roasting changed the antigenic structure and rendered the finished product nonallergenic. The allergic symptoms in their subjects consisted of nasal congestion and discharge, dermatitis, dyspnea, asthma and sore eyes with lachrimation.

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It has been postulated that patients suffering from allergy to green coffee also react to castor beans and that this cross-reaction is mediated through chlorogenic acid which is present in both (Freedman et al., 1961). However, Layton and coworkers (1965) presented evidence, based on skin tests, demonstrating that chlorogenic acid was not a factor in allergy to either coffee or castor. They considered allergy to green coffee as a typical example of hypersensitivity to a specific protein in the coffee and did not find any reaginic reaction to roasted coffee or to the coffee beverage.

In some South and Central American countries the sacks used for the export of coffee are those that have been previously used for the transport of castor beans. Figley and Rawling (1950) suggested that allergy to coffee was due to accidental contamination of the coffee by the castor beans via these sacks. This theory was supported by Bernton (1973) on the basis of a case of asthma in a worker who developed the condition after five and a half months of employment. He had positive skin reactions to castor bean dust as well as to strands from the sack. However, Kaye and Freedman (1961) demonstrated that coffee which had been transported in previously uncontaminated bags caused hypersensitivity reactions.

Van Toorn (1970) described a case of hypersensitivity pneumonitis in a man who had worked for more than 20 years in a coffee roasting factory. This worker, who had dyspnea and cough, showed nodular shadows in his lungs on

chest X-ray and a diffusion defect via lung function tests. The diagnosis was confirmed by immunofluorescent studies and lung biopsy. Another case of diffuse pulmonary fibrosis in a coffee roaster with 20 years of service was described by Decroix and coworkers (1977). Specific serum precipitins were demonstrated in this case.

Zuřkin and colleagues (1979) studied the respiratory function of 72 processors of roasted coffee and 31 processors of green coffee. Bronchoconstriction was reported in both groups of workers, and this was better demonstrated with maximum expiratory flow volumes (MEFV) than with one-second forced expiratory volume ( $FEV_1$ ) or with forced capacity (FEV). This study also showed that exposure to dust from both roasted and green coffee was associated with chronic as well as acute respiratory symptoms during working hours. The chronic symptoms were more common among processors of green coffee than in the other group, suggesting that that dust had a more potent effect on the respiratory system than that from roasted coffee. Asthma occurred in three workers (2.9%) while none of the controls had the condition. This incidence is considerably less than that reported by Kaye and Freedman (1961), namely 7.3%.

Information is not available on characteristics of the dust, environmental exposure data or dose response relationships.

#### 4.2.3.5 Chili

Source and uses. Chili is the pod-like fruit of the small herbaceous shrub, Capsicum, of which there are several species. It is grown in tropical regions such as India and Sri Lanka, the West Indies, Africa, and tropical

America. The word chili is reserved for the pungent varieties which include C. frutescens and C. minimum, and is an essential ingredient in the preparation of tropical dishes. The pungency excites the appetite but tastes burning hot to the uninitiated western palate. The pungent element in chili ~~is capsaicin. Capsicum B.P.C. is used as a carminative and an external~~ irritant. The less pungent variety of capsicum, known as paprika, is grown extensively in Hungary and Yugoslavia. In powdered form it is used in East European countries as a seasoning for food along with table salt and pepper.

The chili plants yield fruits throughout the year. Chili pods are 5-7 cm long and taper to a point at the tip. These pods, which are green when raw, turn bright red upon ripening due to a mixture of carotenoid pigments. When dried in the sun ripe chilies become papery thin but retain their red color and the pungency. Dried chilies can be kept for many months without undergoing spoilage. While fresh chilies are used to some extent in the preparation of food, the main demand is for the red dried chilies in the powdered form. The producing countries are the main consumers of chili, but a sizeable market has also been created by immigrants who have settled in Western countries.

Until a couple of decades ago, the powdering of dried chilies was done manually in individual households. Over the years this strenuous and time consuming method has been replaced by a mechanical process. Now the powdering is done in small mills established in almost every small town throughout the producing countries. It has become a minor industry, employing a few thousand workers. These mills, which are usually electrically powered, employ three to eight workers each. The powdered chili is sold at the mill itself or supplied

to retailers for distribution. Sometimes a household which prefers to use a quality product may get a chili of its own choice powdered at the local mill for a fee. Sometimes chili is roasted before powdering and used for special culinary purposes.

Each establishment has one or more grinding machines. The chilies are fed into a conical hopper mounted on the machine and the powder that comes through a large nozzle below is collected into pails. This powder is run through the machine twice more until the finished product, a very fine powder, is obtained. Packing into polythene bags is usually done by the same workers at the mill.

The mills adopt various measures to increase ventilation. Some have several large windows which are kept open; a few have a ventilation gap between the roof and the top of the wall; and others have a high roof which provides a large cubic capacity for the room. Exhaust fans are usually not fitted to these units.

The farmers who pick ripe chilies from the plants are not exposed to any irritant dust, but workers who dry them in the sun and then pack them into sacks are exposed to such dust to some degree. The workers who are most exposed are the chili grinders who use the mechanical process. Household grinding and use does not entail any significant exposure.

The characteristics of chili dust are not fully known. Its active principle, capsaicin, is extremely irritant to the mucus membranes of the eye, nose, mouth and respiratory tract. Chili powder is a minor irritant even to the intact skin but the discomfort is increased when it mixes with sweat or

Clinical and epidemiological findings. In the only available study on the effects of chili dust, 21 workers from six chili grinding mills in Sri Lanka were investigated (Uragoda, 1967). All were men and their ages ranged from 19 to 40 years, the average being 29. Their employment as chili grinders ~~extended from 6 months to 10 years, the average being 4 years 9 months. Every~~ worker had experienced symptoms on first taking up his employment: sneezing, watering of nose and cough (95%), burning sensation of the body (95%), loss of weight (58%), cold lasting longer (11%), tightness of chest (11%) and hemoptysis (5%).

The combination of sneezing, watering of the nose and cough occurred in 18 men; in three (15%) these symptoms were severe, in five (27%), mild. These symptoms lasted from three days to six months, the average being seven weeks. These symptoms, once they subsided in three of the workers never returned again, but in the remaining 15 there was only relative tolerance, for these came on in a milder form when the dust in the room was disturbed by a breeze coming through the windows, or while grinding roasted chilies. When whole chilies are roasted the active principle, capsaicin, volatilizes and the gas is trapped within the pod. When it is ground soon after roasting, this irritant gas is liberated. A similar type of tolerance has been reported in workers exposed to coffee dust (Zuśkin et al., 1979).

A symptom present as long as they worked was a burning sensation of the body. It was especially noticeable when the skin was moist with sweat which acts as a vehicle for the chili powder.

Eleven men experienced loss of weight ranging from 1.3 to 9 kg, the average being 4.7 kg. It was unaccountable and not consistent with the physical exercise involved in the occupation. Paprika splitters also suffered from this symptom.

Chili powder does not appear to cause any permanent changes in the respiratory system. The symptoms seem to last as long as they worked in the industry. The chest X-ray was normal in all the workers. Skin testing with extracts of chili powder did not reveal any reaction. Serological tests did not show any reactions of a specific nature (Uragoda, 1983).

A fibrosing alveolitis has been reported in paprika splitters. These workers used to split paprika fruits in order to remove the pungent ribs before grinding. These fruits during the later stages of development become infected with a fungus, Mucor stolinifer. During the process of splitting the spores are liberated and inhaled by workers. Lately, a variety of paprika which is devoid of any pungency in the ribs has been developed, and splitting has therefore become unnecessary (Hunter, 1978).

#### 4.2.3.6 Cocoa

Source and uses. Cocoa is obtained from the fruits of the cocoa tree, Theobroma cacao, which grows in tropical regions usually within 20° on either side of the equator. It is a native of Central America but the bulk of the world output is now grown in West Africa, Ghana being the largest producer in the world. Cameroon, the Ivory Coast and Nigeria are the other principal cocoa growing countries in West Africa. Central and South America still

retain a sizeable market, Brazil being one of the largest producers in the region. Cocoa is also grown in the West Indies, the Philippines, Sri Lanka and Western Samoa.

~~Cocoa is used mainly for the manufacture of edible chocolate, potable~~  
cocoa and cocoa butter, and to a lesser extent in the manufacture of theobromine. Cocoa butter constitutes about 56% of good cocoa beans and is a high grade vegetable fat. It is used, along with cocoa powder, in the manufacture of chocolate.

The harvesting season during which ripe fruits are picked extends over several months. Each fruit usually contains 20 to 40 seeds or beans which have an outer mucilaginous pulp. During the fermentation of seeds, microorganisms remove this musilage and thereby facilitate subsequent drying of the beans. The picked fruits are split and the seeds extracted in the field. The seeds are then transported to the factory where they are allowed to ferment for a few days. During fermentation much heat as well as carbon dioxide is liberated. A wide space between the eaves of the roof and the top of the walls in the fermentation room allows the free movement of air and the escape of gases that are generated during fermentation. The beans are then dried either in the sun or artificially and exported.

The United States of America is the world's largest consumer. The other principal consuming countries are Canada, France, Federal Republic of Germany, the Netherlands and the United Kingdom. The Americas and Europe together consume about 90% of the world output.

No estimate is available of the number of workers engaged in the cocoa and chocolate industries, but since production and consumption are worldwide the workforce should be considerable. In addition to cocoa dust the workers in ill-ventilated factories are likely to be exposed to gases liberated during fermentation.

Clinical and epidemiological findings. Williams and coworkers (1973) reported an episode in which 17 longshoremen unloading cocoa beans from the inadequately ventilated hold of a ship developed symptoms within 20 minutes of starting work. Symptoms consisted of nausea, eye irritation, substernal burning chest pain, shortness of breath and labored breathing. They were all admitted to a hospital. One man was found to have a complete heart block which subsequently required an artificial pacemaker. Another required a temporary wandering pacemaker. The remainder recovered uneventfully. It was suspected that the environment to which they were exposed had a low oxygen level, a high carbon dioxide concentration and contained ethyl alcohol and acetic acid as a result of fermentation of the beans.

#### 4.2.3.7 Cinnamon

Source and uses. Cinnamon is the bark of the tree Cinnamomum zeylanicum. It is grown in Sri Lanka and to a lesser extent in South India and the Seychelles. True cinnamon has to be differentiated from cassia which is obtained from the Cinnamomum cassia that grows in China.

It has an agreeable and delicate fragrance and a sweetly pungent taste. Because of these properties it is used as a flavoring agent in confectionary, pharmaceutical preparations, oriental curries, chewing gum, toothpaste, mouth

washes, and cosmetics. Cinnamon oil which is distilled from the bark and leaves of C. zeylanicum and C. cassia contains as much as 68% of cinnamic aldehyde which is an irritant capable of blistering the tongue. However, powdered cinnamon contains only about 1% of the aldehyde.

~~Manufacture. The trees are harvested throughout the year. The bark is~~  
 peeled off the wood after making longitudinal incisions. The separated barks which are in the form of tubes are dove-tailed into each other to form quills 105 cm in length. Broken ends and pieces are inserted into the cavity of the bark. The quills are then dried indoors and bleached to a golden color by exposure to sulfur dioxide. It is exported mainly to Mexico and other Latin American countries.

Clinical and epidemiological findings. Only one study has been done in which 40 workers were examined (Uragoda, 1984). Their average age was 31.8 years and average period of service four years (range 2 months to 11 years). Thirty five workers had symptoms (see the following table).

Table 8. Abnormalities in Cinnamon Workers

Symptoms	Number	Proportion %
Loss of weight	26	65
Irritation of skin	20	50
Loss of head hair	15	37
Cough	15	37
Asthma	9	22
Smarting of eyes	9	22
Skin rash	5	12

Seven out of the nine cases of asthma developed after starting work with cinnamon. A provocation inhalation done in one case induced an attack within ten minutes. The cough and skin irritation were probably due to cinnamic aldehyde. There was no evidence of chronic bronchitis. There was no explanation for the loss of weight which ranged from 1 to 12 kg.

Contact dermatitis due to sensitivity to cinnamon (Tulipan, 1932; Kern, 1960) and cheilitis due to cinnamon oil (Miller, 1941; Laubach et al., 1953) have been reported.

4.2.4 Tobacco and Rice<sup>1</sup>4.2.4.1 Tobacco

Sources of material. Tobacco constitutes a large part of the economic ~~wealth of certain regions and is almost universally an important source of~~ government revenue (Akehurst, 1970; Sangro y Torres, 1983a; Suma'mur, 1982a).

The tobacco plant belongs to the Nicotinae genus of the family, Solanaceae. It has three subgenera (Rustica, Polinoides and Tobacum) and about 60 different species (Akehurst, 1970).

The use of tobacco was observed by Columbus in the West Indies in 1492. It was cultivated as a crop by European settlers in America from the beginning of the 17th century. Owing to its special capacity for adaptation, it is now cultivated over extensive areas of the world ranging from the tropics to the temperate zones. It is grown on large plantations, but much is also produced by small holders (Garner, 1951). There are many tobacco producing countries in the world and the product is used almost everywhere.

World production of tobacco in 1930 was approximately six million metric tonnes according to the UN Statistical Yearbook, 1982. The largest producer is China with 1.5 million tonnes, followed by the USA, India, Turkey. Other large producing countries in order of production are Greece, Indonesia, Zimbabwe, Poland. Turkey, Greece and Bulgaria produce substantial quantities of Turkish or oriental tobacco. The main exporters of unmanufactured tobacco are China and the USA. United Kingdom and the Federal Republic of Germany are

large importers. In 1982, the largest producers of cigarettes were (in millions): the USA: 732 082, the USSR: 359 440, Japan: 309 063, the Federal Republic of Germany: 146 713, Brazil: 133 200, followed by the United Kingdom, India, Indonesia and Poland.

Leaves of a tobacco plant are sessile and decurrent. The water content of the leaf decreases during ripening. Tobacco has a high content of ash, the quantity in dry leaf ranging from 12-25 %. The quantity and composition of the mineral components affect the combustibility of the leaf (Akehurst, 1970). Inorganic elements in tobacco leaf include aluminum, arsenic, barium, beryllium, boron, calcium, cesium, chlorine, chromium, cobalt, copper, fluorine, iodine, iron, lead, lithium, magnesium, manganese, mercury, molybdenum, nickel, polonium, potassium, radium, rubidium, selenium, silicon, silver, sodium, strontium, thallium, tin, titanium, uranium, vanadium and zinc (Tso, 1972).

Tobacco can be manufactured into cigars, cigarettes, pipe or chewing tobacco and snuff. Smoking, an addictive habit, is now practiced throughout the entire world. The alkaloid, nicotine, is extracted from tobacco waste and was formerly much used as an insecticide. On oxidation it yields nicotinic acid, a constituent of many vitamin preparations (Akehurst, 1970). Tobacco is no longer used medicinally in Europe. In some societies, its water extract is used for scalp cleaning or treatment of wounds or lesions.

The fibrous parts of the leaves may be shredded or cut up and added to the leaf of tobacco during the course of manufacture. In some factories, tobacco dust is collected and in others unused residues are burned (Sangro y Torres, 1983a).

Characteristics of dust. Very little information is available on the physical, chemical and biological characteristics of tobacco dust. In one study, Suma'mur (1974) reported that a laboratory analysis on tobacco dust revealed a nicotine content of 2%. Tobacco dust sent to a microbiology ~~laboratory for acid fast bacilli examination and animal inoculation gave~~ negative results.

Sources of exposure in producing and importing countries. Tobacco dust may be generated in the production of tobacco and the manufacture of its products. During cultivation, green and fresh leaves of tobacco do not produce dust. During processing after harvesting, dust may be produced in the storage, handling, and transporting of the dry tobacco leaves. These activities, however, are usually seasonal so that exposures are not continuous. Exposure to tobacco dust is likely in its manufacture, the most exposed workers being processors, cutters, and blenders.

Methods of cultivation vary from region to region according to climate, soil fertility, species of plant, and the type of leaf required. Broadly, the sequence involves deep plowing of the soil, transplanting of seeds from nurseries, hoeing, weeding, application of pesticides and fungicides, and watering during dry seasons. At a certain stage, plants are disbudded or "topped" by the fingernails or small knife and the buds appearing in the angles between stem and leaf are also removed. About two months after fluorescence, the leaves become yellowish and wrinkled and are ready for harvesting. The whole plant is cut down with a sickle or knife or the leaves are removed from the stem with a knife (Sangro y Torres, 1983a; Garner, 1951).

Tobacco leaves are further cured and fermented. Curing may be done in various ways and the processes include: air curing in containers through which currents of air are circulated; sun curing on the walls of houses or on poles; fire curing by smoke from a hardwood; or flue curing in driers with a network of steam or hot-air tubing. Sometimes these procedures are combined. Fermentation is essentially not bacterial but chemical and enzymatic. It can be accomplished by piling up bales of tobacco in an aerated storeroom for three months or storing in air-conditioned chambers for 9-10 days. In certain cases, the tobacco is also aged. After refrigeration, moistening and drying, the tobacco is packed in casks which are kept in ventilated storerooms for one to three years. Classification, sorting, packaging, and bailing are the last stages before the leaf is sent to the factories for manufacture (Sangro y Torres, 1983a).

Many tobacco, cigarette or cigar manufacturing factories are now large and fully mechanized but some of the finest cigars are still made by hand in small establishments, to a large extent by female workers. Methods of treatment vary according to the type of tobacco and the product required, but follow a general basic pattern. Tobacco is received in bales arranged in layers (Sangro y Torres, 1983b; Suma'mur, 1974). The bales are opened and the tobacco is subjected to conditioning and mixing processes which vary according to the type of tobacco and eventual product required. To make handling easier, the water content of the bales is increased by 2-5 % by sprinkling them with water or by putting the bales into steam chambers. The moistened bales are then opened and the fibrous stems of the leaves removed. To obtain the uniform, constant quality of a desired type, different crops of tobacco are mixed on conveyor belts or revolving drums or rotary chests or by shaking on a continuous belt. With the exception of oriental tobaccos, the moisture

content is increased again, usually by warming in revolving drums or heated containers. To improve the quality and to give an aroma, the tobacco is mixed in revolving drums with a large variety of vegetables or chemical substances, called casings. Nicotine is then removed from the tobacco by various methods ~~including passing currents of air over the tobacco at 100°C for 24 hours,~~ electrolysis, electro-osmosis or by a current of ammoniated steam, following which the leaves are cut to shreds of equal size in shredding or cutting machines. To prevent fermentation after cutting, the moisture content is rapidly reduced, first by warming in roasters or drying drums or by "poisoning" followed by cooling in a current of air (Provost, 1959; Sangro y Torres, 1983b).

In modern cigarette manufacture, binding machines wrap up the tobacco in paper to form a continuous cigarette or rod which is cut to the required size. In traditional processes of cigarette production, processed or spiced tobacco is wrapped up by hand using a simple rolling apparatus (Sama'mur, 1974). In cigar manufacture leaves or pieces of leaves are made into a roll which is then wrapped with a leaf of better quality or appearance. The work may be done manually, semi-automatically or fully automatically. In the final stages the cigarettes and cigars are wrapped, assembled, and packaged for sale. Much of the packaging is done by machine, and it is common for the packing material to be made on the premises (Provost, 1959; Sangro Y Torres, 1983b).

There is frequent transport of tobacco inside the factories using, for example, screws, belts, or vibratory conveyors (Sangro y Torres, 1983b). The levels of dust in the production of tobacco products and in particular during tobacco sorting (Breternitz, 1983) depend on the process used, the degree of

ventilation, cleanliness and housekeeping, and personal hygiene. Nonoccupational exposures to tobacco dust may occur in homes if drying of tobacco leaves or cutting is done there.

Clinical findings. Clinically, the most significant respiratory effects are chronic bronchitis and to a lesser degree occupational asthma. For example, Suma'mur (1974) described the symptomatology in a male worker, 49 years old, 154 cm tall and 49 kg of body weight, who had been working for 20 years in a cigarette factory and had chronic bronchitis with respiratory disability of grade II. The affected worker stated the following: "I have been working continuously in cutting tobacco leaves for 20 years. When I started to work in the factory I was perfectly healthy. After 14 years of work, I often suffered from cough, especially on exposure to the dust, and sometimes with fever. Later on, I used to cough at any time rather at home at night or on getting up in the morning and also at work. The cough was productive and lasted for almost all the time. Since four years ago, my ailments have been as such that I have not been able to walk up a slight hill due to shortness of breath. I am now unable to walk keeping up on the level with healthy people. I am a smoker, but only a light one of three cigarettes a day." On clinical examination, his general condition was poor, with a barrel chest and dry rales. X-ray findings indicated no tuberculosis process, but the increased vascular markings and darkened lung fields, together with the clinical signs, suggested chronic bronchitis and emphysema.

Workers exposed to tobacco dust may develop asthma (Suma'mur, 1974). The disease is characterized by dyspnea and wheezing and the severity of symptoms increases with exposure. Lung function tests show an obstructive pattern

which is relieved by bronchodilators. A case report by Gleich and co-workers (1980) indicated an allergy to tobacco. According to Sangro y Torres (1983b), respiratory disorders (in particular dyspnea, emphysema and chronic bronchitis) are similar to those produced by vegetable dusts of low aggressivity.

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Chronic bronchitis and asthma in tobacco workers has been called tabacosis (Schepers, 1980). There has been no common agreement, however, on this terminology. In some literatures, tabacosis refers to a lung disease which belongs to the group of pneumoconioses. Long, as cited by Johnstone (1974), after studying workers exposed to tobacco dust, concluded that pneumoconiosis (tabacosis) does not develop in tobacco workers.

Persons exposed to organic dusts including that of tobacco seem to have a susceptibility to pneumonia (Hunter, 1978). This observation should be further studied. However, there are no indications that tobacco workers are at increased risk for tuberculosis (Suma'mur 1974; Johnstone, 1974).

Among its other effects, tobacco dust can irritate the eyes, upper respiratory tract, stomach, genital mucous membranes in women (Regidor & Losada, 1960), skin, and nervous system. Conjunctivitis, dryness and irritation of the rhinopharyngeal mucosa, and a sensation of fullness of the stomach have frequently been reported amongst new workers. These symptoms disappear after a few days adaptation. Attacks of acute nicotine poisoning with nausea, vomiting, and faintness have been recorded but chronic poisoning is probably only seen where personal and general hygiene is poor (Detroy & Lessenne, 1950; El Batawi, 1983; McCormick et al., 1948; Sangro y Torres,

1983b). In addition to direct contact with tobacco leaves or processed tobacco, the dust may cause a dermatitis (El Batawi, 1983; Sangro y Torres, 1983a; Suma'mur, 1974).

Systemic and nervous system effects include dystonia with an initial phase of excitation of the parasympathetic system, spasm which includes intestinal, hepatic and renal colic, bradycardia and hypotension, depression, menorrhagia and high blood pressure. With high exposure to tobacco dust, Suma'mur (1974) described affected workers experiencing a syndrome consisting of fever, cough, and headache. This syndrome suggests possible irritation to the respiratory apparatus as well as a nicotine and heat stress effect.

Explosions of tobacco dust have been reported (Sangro y Torres, 1983b).

Ramazzini (1713) included the maladies of tobacco workers among occupational diseases suffered by those engaged in dirty and dangerous trades described by Hunter (1978).

Epidemiological findings. Epidemiological studies on respiratory effects of exposures are limited in number (Suma'mur, 1974). Long, as cited by Johnstone (1974), studied a group of tobacco workers over a period of ten years. There were 2 254 persons, of whom 1 246 had been exposed to tobacco dust while working. He concluded that pneumoconiosis (tabacosis) does not develop in tobacco workers. Other investigators (Athayde, 1948; McCormick et al., 1948) have studied tobacco workers but no particular emphasis was placed upon measuring respiratory effects.

Suma'mur (1974) conducted an epidemiological study on respiratory diseases due to exposure to tobacco dust in 12 tobacco factories with 1 559 workers. All the workers had been examined by: interview, using special questionnaires to detect respiratory diseases; clinical and laboratory ~~examinations; mass chest screening followed by large film examination for~~ suspected cases; and measurement of vital and timed vital capacities of the lungs. Respiratory disability was assessed by interview and direct observation of workers' activities. For comparison, morbidity statistics found in preemployment health examinations or in other workers groups were used. Industrial hygiene surveys of the working environment included heat stress levels, noise, and concentrations of dust and gaseous contaminants. Nicotine content of tobacco dust was also determined.

There were 421 (27%) males and 1 138 (73%) females. The majority of the males worked in cutting, blending, packing, and transporting operations, whereas women were generally engaged in rolling. The workers were young with only 2% aged more than 55 years. A third of them had worked less than two years, 32% between two and five years and 35% more than five years. Sixty two (4.0%) workers were nonsmokers, 265 (17.0%) were smokers with less than 10 cigarettes, 86 (5.5%) were smokers with 10 up to and including 20 cigarettes, and 8 (0.5%) smoked more than 20 cigarettes a day. There were 73 cases (4.7%) of chronic bronchitis many with evidence of nonextrinsic asthma, 36 cases (2.3%) of lung tuberculosis and two with nonoccupational bronchial asthma. Compared to the control group, chronic bronchitis was notably higher among the tobacco workers.

Supporting the possibility of an occupational basis of the chronic bronchitis in this population were the following: 1) chronic bronchitis was found in a relatively young population with 50 cases (68%) being under 45 years and 67 (92%) under 55 years old; 2) the number of the affected workers increased with increasing duration of work in the cigarette factory, with eleven (15%) workers with chronic bronchitis being engaged in the cigarette factory two years or less, 22 (30%) five years or less (but more than two), and 40 (55%) more than 5 years; 3) the possibility that smoking was the sole cause of chronic bronchitis seemed unlikely as 37 cases (51%) of the disease were women who did not smoke; additionally, there was no correlation between smoking habits and disease prevalence in the male tobacco workers; and 4) there was, however, a correlation between the number of cases and the dust concentration in the working place. Further, 26 cases or 36% of those with chronic bronchitis had other respiratory disabilities. Of these 26 cases, 18 or 69% had respiratory disabilities of grade I, 6 (23%) grade II, 0 (zero) grade III, and 2 (8%) grade IV. A correlation was suggested between the grade of disability and the length of work in the factory, but statistical computation was not made due to the small numbers of workers (Suma'mur, 1974).

Regarding lung tuberculosis as diagnosed by clinical examination and X-ray film, the incidence rate was 2.3% of the studied population. To appraise the role of tobacco dust in disseminating the disease, dust samples were sent to a microbiology laboratory for acid fast bacilli examination and animal inoculation. No tuberculosis bacilli were detected (Suma'mur, 1974).

A high percentage of workers were found with hyperthermia owing to environmental heat stress within the factories. In addition, a high prevalence of dermatosis was found in the tobacco workers.

Tobacco dust concentrations varied widely in the working environment. Suma'mur (1974) measured dust concentrations in three groups of workers: these were 10, 33, and 96 mg/m<sup>3</sup>. The percentages of chronic bronchitis in these populations were 0.6%, 8%, and 20% respectively. Only one case of chronic ~~bronchitis was detected in the lowest exposed group indicating that the safe~~ level lies somewhere below 10 mg/m<sup>3</sup>. However this conclusions is based on limited data and further studies would be required to establish a definite standard.

Research priorities. Considering the economic importance of this product and the size of the working population, well-controlled epidemiologic studies are indicated to determine the relationship between chronic bronchitis and asthma and exposure to tobacco dust. These need to be complemented with industrial hygiene measurements of total and respirable dust levels so that dose response relationships can be delineated. Detailed analyses of the constituents of tobacco dust are indicated.

#### 4.2.4.2 Rice

Sources of material. Rice is the staple food of over half of the world's population, particularly throughout Asia. It contributes 40% to 80% of the energy values and 40% of the protein in the Asian diet. The annual world output of rice is several hundred million tonnes of rough rice or paddy rice (Suma'mur, 1982b). The biggest producers are Brazil, India, Indonesia, Japan, Pakistan, and Thailand (Grist, 1965; Wongpanich, 1983).

The rice plant is non-woody and has a round, slender, hollow stem and alternate nodes and internodes. The leaves are alternate and are attached to the stem in two rows. The roots are fibrous and develop from the nodes underground. In the floating variety of the plant, adventitious roots may sprout from the stem immediately above ground. The rice flower has both stamens and pistils. (Grist, 1965; Wongpanich, 1971).

There are two main species of rice which are cultivated. They are Oryza sativa in Asia and Europe and Oryza glaberrima in tropical West Africa. Rice is also classified by geographical areas of cultivation. Thus there is the (1) Indica variety -- cultivated in tropical regions of India, Indonesia, and the Philippines -- which yields long- or medium length grain; the (2) Japonica variety -- grown in subtropical areas of Japan, Korea and the north of mainland China -- which produces short length grain; and the (3) intermediate variety -- grown commonly in Burma and Indonesia -- which produces grain intermediate in length. High yield varieties have been introduced in recent years in order to increase production. According to cultivation site, rice is classified into two groups; lowland or irrigated rice, grown in marshy areas only and needing plenty of water, and therefore a rainy season crop, and upland or nonirrigated rice, grown in forest, on plateau or hilly regions. For the latter, irrigation is not necessary as the natural rainfall provides adequate water. (Grist, 1965; Wongpanich, 1971).

The rice grain consists of an edible portion, brown rice, enclosed by the hull. Starch is the major constituent of rice (75%) and is present in the endosperm as compound granules 3 - 10 mm in size. Protein, the second major constituent (8%), is found in the endosperm as bodies 1 - 4 mm in size. The concentration of non-starch constituents is higher in the bran and germ

fraction than in the endosperm (Juliano, 1972). Rice grain is cooked by boiling, steaming or frying, and is sometimes ground to produce rice flour.

Characteristics of dust. Analytical studies of the composition of rice dust have not been performed. ~~Suma'mur (1974) reported dust concentrations in~~ the rice mills ranging from less than 10 to more than 100 mg/m<sup>3</sup>. Margono and co-workers (1980) reported the concentrations of rice dust at storage places varying from 37 to 383 mg/m<sup>3</sup> with an average of 189 mg/m<sup>3</sup>.

In five work areas within a production commune in China, Olenchok and co-workers (1984) measured average concentrations of total and vertically elutriated airborne dust of 15.69 ± 1.91 mg/m<sup>3</sup> and 6.00 ± 1.47 mg/m<sup>3</sup> respectively. Gram-negative bacterial endotoxin levels in air were 492.12 mg/m<sup>3</sup> for total dust and 100.22 mg/m<sup>3</sup> for elutriated dust.

Sources of exposure in producing and importing countries. In producing countries, exposure to rice dust may occur during harvesting and threshing or in milling and transporting. In importing countries, processing, packing, storage and transporting are the main dust producing activities. In all these activities, farm workers and sometimes their families, millers, handlers and rice storage workers are particularly exposed to rice dust. (Suma'mur, 1982b).

Cultivation of rice includes a range of activities such as tilling the soil, weeding, preparation of seedlings, transplantation, harvesting, drying and threshing. Since rice dust is the topic of interest here, only harvesting, drying and threshing are further described. In oriental countries rice is usually reaped by hand when the plant is about 100 days old. A sickle or similar implement is used. In developed countries, rice is usually

harvested mechanically. Harvested rice is then dried in the sun. To avoid the grain cracking when milled, harvesting is done before the moisture content of the grain falls below 15%. The purpose of threshing is to separate the grain, with its husk or glume, from the stalk. The paddy crop is usually threshed immediately after harvesting. Occasionally it requires a short period of sundrying. The rice sheaves are laid two or three deep round a central stake in the threshing floor, with their heads pointing inwards, and buffaloes or oxen then slowly drag the threshing combs over them to force out the grain. (Grist, 1965; Wongpanich, 1971). Threshing is sometimes done by foot or beating. Mechanical threshing is performed in developed countries.

In the rice mill, the rice grains are separated from the husk. The grain and husk are first dried in the sun. The husk is then broken mechanically and separated from the grain. Sieving is the next step to clean the seeds from the light husks. In many areas, this is still done by hand. Work in the mill is generally seasonal and lasts for a few months (Suma'mur, 1974).

As the harvesting and drying operations are done in the open air and the task is seasonal, there is little potential for rice dust exposure. Likewise threshing is usually performed on a small scale by individual farmers on an infrequent basis, thus exposure is unlikely to be high. On the other hand, rice milling is a very dusty operation. (Suma'mur, 1974). Rice dust is also produced in the storage, handling and transporting areas.

Rice is sometimes ground to produce rice flour. Its production is small and before grinding, the grain is first moistened, thus reducing the amount of dust produced (Suma'mur, 1982b).

Clinical findings. Studies on the respiratory effects of exposure to rice dust are limited in number. This fact is surprising in view of the potential frequency and intensity for occupational exposure workers receive in their handling of this fundamental if not ubiquitous food staple (Suma'mur, 1974).

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Schepers (1980) described the most common cereals to which sensitization has been demonstrated as wheat, rye, barley, oats, and buck wheat. No mention was made of rice. In discussing occupational health hazards related to rice, Wongpanich (1971) does not mention the possible effects of rice dust. Clinically, exposure to rice dust results in chronic obstructive pulmonary disease, characterized by persistent cough with phlegm. The disease does not seem to lead to respiratory disability probably because exposures are seasonal and intermittent with dust free intervals allowing recovery (Suma'mur, 1974; Margono et al., 1980). A case of hypersensitivity pneumonitis has been described in a farmer exposed to rice dust (Uragoda, 1967).

Exposure to rice dust may also result in an increased incidence of skin diseases especially if the environment is dusty or if there is a lack of sanitary facilities. The skin diseases are infectious and most of them are due to fungi. In tropical countries, the rice worker may face relatively high heat stress resulting in hyperthermia (Suma'mur, 1974).

Epidemiological findings. There have been only two epidemiological studies on the respiratory effects of exposure to rice dust. Suma'mur (1974) studied 20 rice mills with a total of 457 workers. The study consisted of an interview using special questionnaires to detect respiratory diseases such as chronic bronchitis, bronchial asthma, etc.; clinical and laboratory

examinations; mass chest screening followed by large film where indicated; and measurement of vital and timed vital capacities of the lungs. Since lung tuberculosis was expected to exist in the study population, X-ray diagnosis of a lung disease was only made if tuberculosis had been excluded. Respiratory disability was assessed by interview and direct observation of workers' activities and graded I, II, III, and IV. Concentrations of rice dust were determined. For comparison purposes, morbidity statistics of an unexposed population were used. Of the 457 rice workers, 404 (88%) were males and 53 (12%) were females. Men were engaged in drying, threshing and packing; women in packing alone. Workers more than 55 years old constituted a small percentage (6%).

One hundred seventy-two workers or 38% of the population with less than two years, 157 or 35% between 2 - 5 years, and 128 or 28% more than five years. Smoking habits were as follows: 23% were nonsmokers, 48% were smokers with less than ten cigarettes daily and 22% smoked ten to twenty cigarettes a day. There were 23 cases (5%) of chronic bronchitis, 12 workers (3%) with lung tuberculosis, and no cases of nonoccupational asthma. The occupational origin of the chronic bronchitis was indicated by the fact that 61% of the cases were under 45 and 87% were under 55 years of age. Unfortunately, a correlation between the number of the affected workers and duration of work in the mill could not be elucidated. The prevalence of chronic bronchitis was high in workers who smoked 10-20 cigarettes a day. There were also one male and one female nonsmokers who suffered from the disease. No case of respiratory disability was detected in the rice workers. Rice dust concentrations in the air were relatively high and ranged from less than 10 to more than 100 mg/m<sup>3</sup>.

Margono and co-workers (1980) studied 159 male rice storage workers and used 59 unexposed persons as a control group. The study consisted of an interview, health examination, lung function test, skin allergy test, eosinophil count, chest X-ray, laboratory examination for acid fast bacteria, and dust measurement. ~~The control group was older than the rice workers.~~

Symptoms of chronic bronchitis were found in 36% of the workers and abnormal lung function of the obstructive type was found in 35% of the workers. In the control group, chronic bronchitis was found in 29%. Statistically, however, this difference was not significant due to the relatively small populations. Smokers comprised 76% of the total work force, and 41% of these laborers who had worked more than five years had chronic bronchitis. Positive skin allergic tests to different fungi were higher in rice storage workers than the control group. This was particularly noticeable for Aspergillus.

Dust concentrations ranged from 37 to 383 mg/m<sup>3</sup> with an average of 189 mg/m<sup>3</sup>. Respirable dust comprised 40% of the total weight. Rice dust was estimated to contain 35% inorganic and 65% organic matters. It was also concluded that participation in sporting activities had a positive effect on health of the workers. Lung tuberculosis was found in 6% of the rice storage workers. This prevalence rate was comparable to the control group. In the other study in the rice mills, Suma'mur (1974) found dust concentrations lower than 30 mg/m<sup>3</sup> in eight out of 10 of the workplaces. Due to the small numbers of workers in these working places, no attempt was made to correlate the prevalence of chronic bronchitis with the dust level.

Research priorities. In view of the economic importance of this industry, controlled epidemiologic studies are required to determine whether rice dust causes chronic bronchitis. These studies need to be combined with industrial hygiene measurements of total and respirable dust so that dose response data can be generated. Detailed analyses of the composition of rice dusts are indicated.

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## 5. METHODS OF INVESTIGATION

### 5.0 Introduction<sup>1</sup>

Methods of investigation provide information regarding surveillance, ~~epidemiology, and research into the diseases related to exposure to~~ agricultural and other natural dusts. Certain techniques have been shown to provide reliable associations with disease and should be recommended as routine. Others, still of research status, may become routine as more information about their utility is gathered. Still other techniques provide only research-related information. Changes in parameters should not de facto be interpreted universally as a sign of disease. Other factors, such as definition of the disease presence and definition of study groups, should be accomplished before testing and subsequent interpretation are accomplished. It is recommended that the first tool to be utilized is an appropriate questionnaire. Administration, collection, and interpretation of questionnaire data are less expensive but oftentimes more useful than more elaborate testing such as pulmonary function assessments, clinical laboratory analyses, or chest radiography.

### 5.1 Human Laboratory Assessment<sup>1</sup>

The American Thoracic Society (ATS) appointed three subcommittees to prepare proposals for questionnaires on respiratory symptoms, the use of chest

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<sup>1</sup>By Major, P.C. & Olenchok, S.A.

radiographs for epidemiological studies and standardization of lung function tests. These were consolidated by the Principal Investigator of the ATS Epidemiology Standardization Project and published in a special issue of the American Review of Respiratory Disease (Ferris, 1978a). The three aspects of the project will be considered separately in the various subsections below.

#### 5.1.1 Respiratory Questionnaire Appraisal

The establishment and standardization of a questionnaire to assess respiratory diseases due to agricultural and other natural dusts are of obvious importance. Inter-laboratory and inter-questionnaire differences should be reconciled in such a manner that accurate comparisons can be made. Questionnaires serve two main purposes. If presented at one time only, they can assist in the determination of prevalence of symptoms, status of pulmonary function, and other related aspects of disease in an initial or cross-sectional study (Ferris, 1978b). Secondly, if the information is obtained repeatedly on the same population, questionnaire information can help to determine the incidence of disease or the progression of illness in a prospective or longitudinal fashion (Ferris, 1978b). A committee from the American Thoracic Society (ATS) together with the Division of Lung Diseases of the US National Heart, Lung, and Blood Institute (DLD) developed recommended respiratory disease questionnaires for use with adults and children in epidemiological research. It is to the published document that the reader is directed (Ferris, 1978b). This questionnaire represents a modification of the Medical Research Council (MRC) standardized questionnaire (MRC, 1960). Major question areas include those relating to: cough, phlegm, episodes of cough and

phlegm, wheezing, breathlessness, chest colds and chest illness, past illness, occupational history, tobacco smoking, and family history. In addition, supplemental questions relating to general demographic data, residence, home heating and fuel were included in the adult questionnaire. The report lists the rationale and justification for the various components of the

~~questionnaire as well as specific instructions for the use of the required~~

questions. Questionnaires were field tested on a relatively small number of normal subjects, and the committee tentatively approved the result. As a final note, the ATS-DLD report states:

"... as hypotheses about the nature and risk of developing chronic respiratory disease change, some questions considered as standard and essential at the present time will become obsolete and useless, whereas others not currently considered as part of the required standard may become more important." (Ferris, 1978b)

Questionnaires which have a long tradition or which correlated well with physiologic or laboratory methods or with disease prognosis oftentimes can be used to identify the presence of a disease or syndrome. Recently adopted questionnaires may be of less immediate usefulness until properly field tested and analyzed. Because the major diseases which are associated with exposures to agricultural dusts (occupational asthma, hypersensitivity pneumonitis, and chronic obstructive pulmonary disease) differ, appropriate questionnaires may be different also. It is suggested, therefore, that the two standardized questionnaires which were discussed, in addition to other questionnaires which are in use currently, be used by the investigator as starting points for the

development of the specific and appropriate questionnaire. Until a standardized questionnaire for agricultural dust-induced diseases is developed, it is suggested additionally that sharing of existing questionnaires and experiences be conducted.

#### 5.1.2 Pulmonary Function Appraisal

Assessment of pulmonary function is a necessary and important component of studies relating to agricultural dust-induced disease (Morgan, 1984; Cotton & Dosman, 1978; Dosman & Cotton, 1978). Inter-laboratory and intra-laboratory results from pulmonary function testing must be comparable in order to document any association between respiratory alterations and dust exposures.

The Division of Lung Diseases of the National Heart, Lung, and Blood Institute contracted with the American Thoracic Society to recommend standardized procedures for pulmonary function testing. Their final document, in collaboration with a number of major groups, was published (Ferris, 1978c) and provides the recommended procedures, calibrations, and rationale for epidemiological investigations.

Minimal requirements for epidemiological studies include forced vital capacity (FVC) and 1-second forced expiratory volume ( $FEV_1$ ) measurements. For interstitial lung disease studies, the carbon monoxide diffusing capacity by the single breath method ( $DL_{CO_{sb}}$ ) may add additional information. Optional tests are maximal midexpiratory flow ( $FEF_{25-75\%}$  of FVC); and maximum expiratory flow ( $V_{max}$ ), flow volume curve.

Supplementary pulmonary function tests include: total lung capacity (TLC) and two of its subdivisions (residual volume [RV] and functional residual capacity [FRC]); maximal voluntary ventilation (MVV); closing volume and closing capacity; and measurement of lung mechanics (although this is not recommended for epidemiological studies). Short-term changes in pulmonary ~~function (FEV<sub>1</sub> or peak expiratory flow) over a workshift can provide~~ information concerning acute effects while long-term changes (longitudinal studies) may be useful in detecting chronic effects.

Standardization of spirometry testing alone is reported further as a separate American Thoracic Society statement (ATS, 1979) and in the United States Cotton Dust Standard as recommended by NIOSH (CFR, 1980). As additional reference, standardization of pulmonary function assessments of individual patients and not for epidemiologic investigations can be found in the report by the Intermountain Thoracic Society (Kanner & Morris, 1975). It should be noted that local prediction equations should be developed for use as a normal or reference population, and appropriate control groups should be used in order to ensure that the local populations match the prediction equations. In addition, the same methods should be used in collecting data for both the reference and study populations. For example, the ATS/NIOSH spirometry standard recommended the use of the largest FVC and FEV<sub>1</sub> regardless of the curve(s) on which they occur. However, many reference population studies have used the average FVC of the best three trials, which may give lower values.

### 5.1.3 Clinical & Research Laboratory Appraisal

Clinical and research laboratory assessments of exposure to agricultural dusts can be used as supportive evidence, specific diagnostic criteria for disease, monitors of the course and progression of disease, or as invaluable research tools.

Immunological Evaluation. Exposures to agricultural dusts may elicit different types of physiologic effects on the subject. However, the unifying thread for the various types of exposures/responses is that agricultural dusts induce or alter an immunological response. This response, while mounted in defense of the lung, often carries a detrimental effect, inflammation with subsequent respiratory pathophysiology.

A number of alternatives may be used to group the types of immunologic assessments which could be used in support of diagnosis and research related to exposures to agricultural dusts. One might choose a disease-oriented approach, the now classical Coombs and Gell (1975) classification, a target organ immunologic assessment, or any of a large group of other approaches. During May, 1981, the Clinical Immunology Committee of the International Union of Immunological Societies (IUIS) and the Immunology Division of the World Health Organization (WHO) assessed general and widely used immunologic determinations (IUIS/WHO, 1981). Because of its relevance to immunologic testing in agricultural dust-induced disease, a similar approach will be followed in this section. Certain determinations which were not discussed by the IUIS/WHO (1981) working party will be added due to their special

significance to research pertaining to agricultural dusts.

(i) Serum immunoglobulin levels. Quantifiable differences in serum concentrations of immunoglobulins can be attributed to sex, ethnic group, age, smoking, and geographic distribution. Consequently, it is recommended that, ~~for research and clinical applications, each laboratory should develop its own~~ normal or reference population levels and not rely solely on published values (IUIS/WHO, 1981). Although this Section deals with serum immunoglobulin levels, most techniques can be adapted to analyze levels of the appropriate agent in lung lavage fluids.

Readily available techniques used to measure immunoglobulins G, A, M, and D can range in sensitivity, complexity, and expense. They include, for example, radial immunodiffusion in gel, nephelometry, rocket electroimmunoassay, and fluorescent immunoassay (IUIS/WHO, 1981; Jackson & Davis, 1980; Nguyen & Dockhorn, 1981). Investigations have shown that analysis of mean immunoglobulin levels for diseased and exposed groups may have significance in certain non-agricultural dust immunotoxicologic assessments (Hahon et al., 1980; Olenchok et al., 1983) as well as agricultural dust-related diseases (Patterson et al., 1973; Roberts et al., 1973). However, the overall value of quantification of the classes of serum IgG, IgA, IgM and IgD is of only limited clinical relevance (IUIS/WHO, 1981), and is not recommended as a routine procedure.

Analyses for the presence of specific antibody, most notably serum precipitating antibody of the G and M classes, are commonplace in research and

clinical determinations of agricultural dust-induced diseases (Pepys, 1969; doPico et al., 1977, Gruchow et al., 1981). Techniques commonly include single and double radial immunodiffusion in gel (Crowle, 1980), rocket electroimmunoassay (Crowle, 1980), and counterimmuno-electrophoresis (Gordon et al., 1971). Although of less common usage, the extremely precise and sensitive methods of enzyme-linked immunosorbent assay (ELISA) (Voller et al., 1980) and radioimmunoassay (RIA) (Parratt et al., 1982) are gaining popularity for research involving minute amounts of specific antibody (Marx & Gray, 1982). Characterization of the precipitin response can be achieved by the more demanding technique of crossed immunoelectrophoresis (Treuhaft et al., 1979; Crowle, 1980). It should be noted that, although specific precipitating antibodies may play some role in the etiology of agricultural dust-induced diseases, controversy exists. It is felt currently that precipitins represent a measure of exposure to antigen and should be considered along with other (historic, radiographic, and immunologic) information as supporting evidence of the presence of disease (doPico et al., 1978) Burrell & Rylander, 1981). Double radial immunodiffusion in gel provides clinically relevant information and is of sufficient sensitivity to be recommended for routine testing provided the appropriate antigen is available (Salvaggio, 1987).

Laboratory analysis for the presence of serum IgE serves as supporting evidence for the diagnosis of allergic disease. While IgE is the most important mediator in allergic/atopic disease, quantification of total serum IgE is often of limited value (IUIS/WHO, 1981). ELISA and solid phase radioimmunoassay are the preferred methods for determining total IgE levels because the radial immunodiffusion method often provides sensitivity and

usefulness only in the ultra-high serum ranges. Both ELISA and paper radioimmunosorbent tests (PRIST) are of high specificity, but PRIST is of greater sensitivity for assaying total IgE (IUIS/WHO, 1981; Adkinson, 1980).

The measurement of antigen-specific IgE is an invaluable tool in the ~~study of allergic, asthmatic, and hypersensitivity reactions to agricultural~~ dusts. Direct binding radioallergosorbent tests (RAST) and ELISA procedures are the most common and available assays (IUIS/WHO, 1981; Adkinson, 1980). Both are well suited for clinical, research, and field investigations and may provide supportive diagnostic criteria for agricultural dust-induced diseases. The RAST assay has additional usefulness in determining the presence of minute amounts of specific allergen. The technique is described as the RAST-Inhibition assay and provides an accurate measure of specific allergen in a mixture of materials (Yman et al., 1975), but it is of research status in the study of environmental or occupational dusts.

Any discussion related to the determination for specific precipitating antibody or allergen-specific IgE must mention the quality of the antigen (IUIS/WHO, 1981). This concern for specific, pure, characterized, and standardized antigen is acutely pertinent to agricultural dusts which are by nature heterogeneous. Commercial antigenic material is oftentimes not available or inappropriate for use with agricultural dust-induced illness. The need for uniform standardization of environmental antigens must be stressed (Aas, 1975; Fink et al., 1977; Federal Register, 1977; Ribon & Gavencak, 1978).

(ii) Complement assays. Quantification of serum complement levels can be obtained by immunochemical measurement of individual components, functional measurement of the whole system, or functional measurement of individual components (IUIS/WHO, 1981). Commercially available antisera against the most common components of the classical and alternative pathways provide relatively simple immunochemical assays by radial immunodiffusion in gel, nephelometry, rocket electroimmunoassay, and fluorescent immunoassay (IUIS/WHO, 1981; Olenchok et al., 1983). Recently developed radioimmunoassays provide opportunities to quantify plasma levels of the complement anaphylatoxins (C3a, C4a, and C5a) as well (Hugli & Chenoweth, 1980). Functional, hemolytic methods for evaluating the total complement system can be performed by the standard tube technique ( $CH_{50}$  u/ml) or by radial diffusion and subsequent lysis of sensitized erythrocytes in gel ( $CH_{100}$  u/ml). Both hemolytic techniques for total complement levels are adapted easily to population studies (Olenchok et al., 1981a; Olenchok et al., 1981b), although the radial diffusion hemolytic technique has been described as a screening procedure for use before the tube technique (Gewurz & Suyehira, 1980). Hemolytic techniques for individual complement components are sensitive and provide functional information rather than immunochemical analysis of break-down products of complement activation. Although hemolytic studies of individual component function are adaptable to population research (Olenchok, 1981), they are more expensive in terms of time, money, and blood sample.

Analysis of serum complement, either immunochemically or functionally, provides a static measurement of the balance between synthesis and consumption of the components (IUIS/WHO, 1981). Oftentimes, single assessments can

provide only minimal information. This situation can be corrected by quantifying components and/or total activity before and after an exposure to an agricultural dust (Olenchock et al., 1981a; Olenchock, 1981). Assays for C4, C3, Clq, Factor B, and properdin are of the greatest clinical and research value because the classical and alternative pathways can be studied and differentiated (Gewurz & Suyehira, 1980; IUIS/WHO, 1981; Olenchock et al., 1981a). Research related to a variety of agricultural dusts implicates the potentially contributory role of complement in the initiation or exacerbation of disease (Edwards et al., 1974; Marx & Flaherty, 1976; Kutz et al., 1979; Olenchock et al., 1980; Olenchock et al., 1981a). As discussed concerning immunoglobulin quantification techniques, complement analyses can be adapted for study of lung lavage fluids, and components of both the alternative and classical pathways are present in human airways (Robertson et al., 1976; Reynolds et al., 1977; Ackerman et al., 1978). However, clinical assessments of complement levels are primarily of research interest.

(iii) Circulating immune complexes. Injury to the lung due to immune complexes was the subject of a review by Daniele and coworkers (1981). Evidence suggests that immune complex deposition can elicit injury to the lungs (Brentjens, et al., 1974; Ward, 1979; Daniele, et al., 1981). Various techniques for the detection of circulating immune complexes have been developed, but the most confidence in positive results can be found in four major tests: Clq binding; conglutinin assays; monoclonal rheumatoid factor inhibition; and Raji cell (using the Raji lymphoblastoid tumor line) assays (IUIS/WHO, 1981). These tests provide research capabilities of modest interest to agricultural dust-induced diseases, but are probably of minor

clinical significance (Theofilopoulos, et al., 1980; IUIS/WHO, 1981).

(iv) Fibronectin. Fibronectin is a glycoprotein which is found in plasma and tissues and is a major adhesive and opsonic agent. Increased levels were shown in bronchoalveolar lavage fluids from patients with interstitial lung diseases (Rennard & Crystal, 1981), and the human alveolar macrophage has been shown to synthesize and secrete fibronectin (Villiger et al., 1981) and thereby recruit fibroblasts to sites of tissue injury (Rennard et al., 1981). Laboratory assessments can be performed on peripheral blood plasma as well as lung lavage fluid. Fibronectin levels can be quantified by enzyme-linked immunosorbent assay (ELISA) (Rennard et al., 1980) and by commercially available turbidimetric techniques. As more is learned about the contribution of fibronectin to the development or exacerbation of lung disease due to agricultural dusts, this potentially powerful research tool may develop clinical significance.

(v) Acute-phase Serum Reactants. In addition to complement, other acute-phase serum reactants have potential importance in research related to agricultural dust-induced disease. Alpha<sub>1</sub>-antitrypsin is probably the best documented agent in terms of its deficiency and disease (Kueppers & Black, 1974; Morse, 1978), although as an acute-phase reactant its level can increase considerably (Kueppers & Black, 1974; Ashley et al., 1980; Olenchock et al., 1981b; Broder et al., 1983). Techniques to quantify immunochemically serum levels of alpha<sub>1</sub>-antitrypsin include radial immunodiffusion in gel and rocket electroimmunoassay, both of which are accurate, reliable, and require small amounts of serum. Applicability to research-related investigations in

agricultural dust-induced disease is seen with alpha<sub>1</sub>-antitrypsin as an acute phase reactant (Ashley et al., 1980; Broder et al., 1983) and in deficiency or variants as detected by low levels and phenotyping (Chan-Yeung et al., 1980; Horne et al., 1980) may hold future promise in defining high-risk groups as may functional assays for alpha<sub>1</sub>-antitrypsin.

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Another useful indicator of inflammation is measurement of the acute-phase reactant, C-reactive protein (CRP). Serum levels elevate within hours of the inflammatory stimulus, peak during the acute response, and return to normal with the resolution of the insult (Wicher, 1980). Commonly used methods for quantifying CRP include precipitation in fluid (Broder et al., 1983) and precipitation in gels, including radial immunodiffusion (Flaherty et al., 1976) and rocket electroimmunoassay (Mattsby & Rylander, 1978). Minimal detectable limits vary with the different techniques and the most sensitive method is radioimmunoassay (Wicher, 1980).

One additional acute-phase reactant which is still in the experimental stage for defining lung injury is haptoglobin (Baseler & Burrell, 1981). Plasma haptoglobin levels, expressed in terms of hemoglobin binding capacity, may prove to be a reliable and consistent determination of pulmonary inflammation (Baseler & Burrell, 1981), although more research and clinical trials are needed.

(vi) B and T Cell Determinations. Characterization of B-cell and T-cell populations and concomitant determination of T-cell sub-populations can be performed on peripheral blood leukocytes and bronchopulmonary lavage

cells. Although these determinations have been essentially disappointing for most clinical purposes (IUIS/WHO, 1981), their role in research and population studies is proving to be fruitful. B-cell populations can be enumerated by identification of the surface membrane immunoglobulins (Horwitz, 1980; IUIS/WHO, 1981). This identification is performed most commonly with fluorochrome-labeled antisera against immunoglobulin Fab fragments, kappa or lambda light chains, or specific immunoglobulin heavy chains. Observation of specific fluorescence provides a simple and reproducible technique. Antibody to specific immunoglobulins has also been coupled to beads (immunobeads), enzymes, radionuclides, and erythrocytes (EAC rosettes) in order to identify specific antibody-forming cells or B-cells in general.

Enumeration of T-cell populations is performed by two recommended research methods, E-rosette formation or the use of T-cell specific monoclonal antibody (Horwitz, 1980; IUIS/WHO, 1981). With the advent of monoclonal antibodies which are directed against distinctive T-cell markers (Kung et al., 1979), T-cell sub-populations such as helper cells and suppressor cells can be identified readily by cytotoxicity tests, fluorescence labeling, or cell sorting techniques. In addition, monocytes can be examined by monoclonal antibody techniques as well. The major draw-back for such testing is, of course, the great expense of the monoclonal antibodies or necessary equipment.

The recognized role of the cellular immune response in the lung (Green et al., 1977; Schatz et al., 1979; Hunninghake et al., 1979; Brownstein et al., 1980) and the search for reasonable animal models of disease due to agricultural dust inhalation (Roberts & Moore, 1977) have stimulated research

concerning the immune cellular populations in animal models (Peterson et al., 1979; Bernardo et al., 1979; Ratajczak et al., 1980) and human subjects (Flaherty et al., 1976; Reynolds et al., 1977; Valenti et al., 1982). In addition, consideration should be directed to the evaluation of functional secretions and responses of lymphocytes from patients with lung disease (Morell et al., 1982) and the effect of agricultural dusts on normal cells (Lewis et al., 1982). The list of mediators of cellular immunity is ever-increasing as research into these potent agents becomes refined (Rocklin, 1982), and techniques to assay most agents as well as B and T cell functions are available (Rose & Friedman, 1980; Yoshida, 1980; Bacon & Heinzerling, 1980).

(vii) HLA antigens. Detection of HLA antigens can provide useful genetic information in population studies or hereditary epidemiology within families. The testing for these markers, HLA-A, B, C and DR, is mentioned here because studies have been performed in patients with bronchopulmonary aspergillosis (Flaherty, et al., 1978) pigeon breeder's disease (Rodey, et al., 1979), and farmer's lung disease (Flaherty, et al., 1980). While those studies were unable to find genetic association with the various diseases, possible genetic factors are proposed in patients with chronic air-flow limitation (Kauffmann, et al., 1983). At this point, however, HLA testing appears to have use only as a potential research tool which is not directly applicable to agricultural dust-induced disease.

(viii) Gram-negative bacterial endotoxins. Laboratory assessment for the presence and quantification of gram-negative bacterial endotoxins is of

importance to the environmental evaluation of the respiratory exposures of workers in agricultural dust-related industries. Inclusion of this assay under this section occurs out of convenience, because it is often performed by the microbiologist or immunologist. The currently accepted method for quantifying the presence of endotoxins is by the Limulus amebocyte lysate gel test. This test is performed commonly by the tube clotting technique and the more sensitive and objective spectrophotometric modification (Olenchock et al., 1982). More recent advances in endotoxin analyses demonstrate the utility and sensitivity of the quantitative chromogenic Limulus amebocyte lysate test as the recommended state-of-the-art for laboratories with the appropriate equipment (Friberger et al., 1982; Pependorf, 1986). The materials are available commercially or the lysate from the horseshoe crab can be harvested and processed in the laboratory. Modifications to the standard techniques have been reported (Jorgensen & Alexander, 1981; Melvaer & Fystro, 1982), but must be viewed with caution until their applicability, sensitivity, and reproducibility are confirmed. The marked biological effects of endotoxins are well documented (Morrison & Ulevitch, 1978), and endotoxins are present in agricultural dusts associated with animal confinement units (Dutkiewicz, 1978; Thedell et al., 1980), animal processing plants (Olenchock et al., 1982), compost (Lundholm & Rylander, 1980), and cereal grains (Dutkiewicz, 1978; Olenchock et al., 1980). Because of the universal presence of endotoxins in these and other agricultural dusts, such as cotton, the presence and quantification of endotoxin should be considered in both laboratory and environmental testing. Dusts may be collected by personal, area, or high volume samplers, and the filter used for collection appears to make little difference in the results if handled properly and the appropriate control

filters are analyzed (Popendorf, 1986).

Hematological Evaluation. Hematological evaluation of peripheral blood can provide valuable and dynamic estimations of systemic alterations because of agricultural dust exposures. It is essential, however, that the blood samples be collected properly with the correct materials, necessary anti-coagulants, and handled properly after collection. Specialized and sophisticated analyses often require special handling of the blood sample and care must be taken to follow the requirements of each procedure. Assays for erythrocyte counts, leukocyte counts, and differential staining and counting of leukocytes are standardized, as are those for specialized staining and cell examination (Davidsohn & Nelson, 1969; Fox et al., 1982). As with all clinical testing, good laboratory practices of standardization should be practiced. Leukocytosis developing with time and accompanying increases in polymorphonuclear leukocytes have been reported after exposure to agricultural and other organic dusts (Flaherty et al., 1976; Rylander et al., 1978; doPico et al., 1982; Parkes, 1982), thus emphasizing the usefulness of hematologic examination for research and clinical appraisals. As a final note, research laboratory animal studies demonstrated associations between peripheral platelet levels and respiratory change after exposure to fungal spores (Burrell & Pokorney, 1977; Olenchok et al., 1979). Measurement of this parameter is of research interest in hematological examinations of patients after exposure to agricultural dusts.

Radiological Evaluation. Questionnaire administration, pulmonary function assessment, and laboratory evaluations are relatively simple to

include in epidemiological studies. Chest radiographs, on the other hand, contribute significantly to the difficulty and cost of field-based research (Ferris, 1978d). Whether performed in epidemiological situations away from the laboratory or in the hospital/laboratory environment, chest radiographs should be of consistently high quality, and of consistent reading and reporting. The most experience with standardization of reading and reporting chest radiographs can be found with the ILO classification for the pneumoconioses (ILO, 1980). The American Thoracic Society and Division of Lung Diseases of the National Heart, Lung, and Blood Institute's epidemiology standardization project used the ILO experience as the basis for developing recommendations, rationale, and instructions for the use of chest radiography in epidemiological studies of nonoccupational lung diseases (Ferris, 1978d). For lung diseases which are induced by agricultural dust exposures, the point at which the radiograph is taken during the course of the disease can help in defining the severity and in differentiating acute from chronic involvement (Parkes, 1982). Chest radiographs may be uninformative in certain agricultural dust-induced diseases such as byssinosis or because of the temporal relationship between radiograph and disease course.

Morphological Evaluation. Examination of tissue specimens provides important information on the type of disease, its severity and the relationship between the suspect agent and tissue response. Direct correlations between the functional and radiographic features of the disease and the anatomic changes in the lungs can also be made. Techniques available to the pathologist include light and electron microscopy, microanalytical procedures and morphometry (Green et al., 1983). Special stains, polarized

light and immunofluorescent and immunoperoxidase procedures are useful adjuncts to light microscopy and, in addition to providing detailed characterization of the tissue response, can also aid in the identification of organic materials within tissue sections. Sub-cellular and surface pathology are best revealed by transmission and scanning electron microscopy, respectively. ~~Electron microscopy used in conjunction with backscattered electron imaging, X-ray microanalysis and selected area electron diffraction may aid in the identification of minerals associated with organic dusts (Abraham, 1978).~~

These techniques can be applied to surgical or autopsy specimens and to cell preparations derived from pulmonary lavage or sputa. Correct methods of fixation and the selection of appropriate controls are very important. For adequate assessment of airways disease and emphysema, it is necessary to fix the inflated lung. The tissues are then processed using routine procedures. Permanent whole lung sections can also be prepared according to the method of Gough (Gough et al., 1949), and a technique has been described also for fixation of surgical specimens in the inflated state (Brody & Craighead, 1975). If electron microscopic studies are indicated, standard procedures for fixation and sample preparation will usually suffice. However, if microanalysis is required also, more complex procedures are indicated (Green et al., 1983). Morphometric (stereological) procedures are useful for quantitative assessment of disease parameters. Many methods have been described and selection of appropriate methods will depend on the specific research need.

## 5.2 Environmental Assessment<sup>2</sup>

### 5.2.1 Worker Exposure Appraisal

The respiratory tract is the major site of injury for most of the dusts described in Table 1. Depending on the size of the particulate, the breathing rate and volume, and the frequency of breathing, the site of deposition may vary. Particles deposited in the tracheobronchial region have been associated with asthma or symptoms of chronic obstructive lung disease. Particle deposition in the non-ciliated regions of the lung, i.e., the respiratory bronchioles and alveoli, is associated with various types of symptoms reflecting response within the alveoli, such as emphysema and the pneumoconioses.

Particle deposition in different regions of the respiratory tract is also related to particle residence time. In the tracheobronchial region of the healthy adult, the residence time of most deposited particles is no more than a few days. In the non-ciliated portions of the lung, particle clearance is not as effective and particle residence time may extend beyond several months. In addition, particles phagocytized in this region may end up in the lymphatic system. Solubility of the particle, or any toxic agent that is part of the particle (i.e., adsorbed gas or pesticides), may also determine whether a pulmonary and/or systemic response will occur.

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<sup>2</sup>By Noweir, M.H., McCawley, M.A., & Hewett, P.

Table 1 - Occupational Exposure to Non-Byssinotic  
Producing Vegetable Dust.

Exposure	Occupations	Major Dust Component	Effect
Grain Dust	Grain elevator workers workers and Grain handlers	Plant fragments, earthy materials, insect mite debris & fungi (e.g. <u>Asper-</u> <u>gillus, Penicillium, Sacor,</u> <u>Rhizopus, Sitophilus grainrius</u>	OA COPD HP
Wood dust	Lumber and wood workers  Board makers  Timber and saw mill workers (Maple bark stripper's disease) Redwood workers (Sequoiosis)	Red cedar and Iroko wood chips Moldy wood chips (e.g. <u>Alternaria SP</u> ) Moldy maple bark ( <u>Cryptostroma corticale</u> )  Moldy redwood dust ( <u>Pullularia</u> )	OA HP COPD?
Hay dust	Farmers (Farmers lung)	Moldy hay ( <u>Micropolyspora</u> <u>faeni</u> and other organisms)	OA
Rice dust	Farm workers (Millers and handlers)	Plant and earthy materials and mold	COPD OA
Tea dust (Black, Herbal, Green, Yellow)	Tea processors, Blenders and packers	Plant and leaf fragments Fermentation products, molds, earthy materials	OA? COPD
Coffee dust (Green or Roasted)	Coffee processors Blenders and packers	Plant and seed fragments, Earthy materials	OA COPD?
Cocoa	Cocoa processors and packers	Plant and seed fragments Earthy materials	COPD HP?
Tobacco	Tobacco processors, Cutters and blenders	Plant and leaf fragments Mould, Earthy materials	OA COPD

Table 1 - Continued.

<u>Exposure</u>	<u>Occupations</u>	<u>Major Dust Component</u>	<u>Effect</u>
Sugar cane dust	Sugar cane workers Paper and board makers	Plant fragments, Mold ( <u>T. sacharii</u> )	HP
Kapock dust	Ginnery, bedding and Upholstery workers	Plant and earthy materials and Micro-organism	COPD OA?
Coir (Coconut husk)	Brush and rope makers	Coconut fiber fragments and earthy materials	COPD
Natural resins and gums (Colophany, Acasia, Karaya)	Solders (Electronics) Printers and paper products manufacturers	Resin dust, vapor of volatile constituents	OA COPD
Caster bean, flax, seed and cotton seed dust	Products of vegetable oil	Seed and plant fragments, earthy material and micro- organisms	OA
Orris Root and other vegetable dyes	Beauticians, cosmo- tologists	Orris root and vegetable fragments; chemicals (e.g. paraphenyline diamine, sodium and potassium persulphate	OA
Tamarind seed	Weavers		OA
Paprika seed	Paprika stripping and Paprika grinding	Moldy paprika ( <u>Mucor stolofiner</u> ) Paprika dust	HP
Chili	Grinders and handlers		COPD
Mushroom dust	Mushroom workers	Moldy mushrooms ( <u>Thermo- actinomyces vulgaris</u> )	HP

Table 1 - Continued.

<u>Exposure</u>	<u>Occupations</u>	<u>Major Dust Component</u>	<u>Effect</u>
Malt dust	Brewery workers and Farm workers	Moldy malt ( <u>Aspergillus claratus</u> )	HP
<del>Cork dust</del>	<del>Cork workers</del>	<del>Moldy cork dust (<u>Penicillium frequentans</u>)</del>	
Pollens	Florists, Horticulturists	Pollens	OA
Proteolytic enzymes	Producers of food additives, detergent makers	Proteolytic enzymes	OA COPD
Tartrazine	Food processors	Food additive	OA
Cheese mold dust	Cheese workers (Cheese worker's lung)	Cheese molds ( <u>P. caseii</u> )	HP
Animal Danders Excreta and Endotoxins	Animal Breeding (e.g. Rodent handlers, lab technicians) Bird handling (e.g. poultry, pigeons, parrots, turkeys, etc.	Danders Excreta (e.g. urine) Endotoxins with vegetable dust	OA HP COPD?
Feathers	Pluckers, Sorters, Bedding, etc. makers	Feathers fragment, Animal Danders and Excreta	OA COPD
Hoja (invertebrate from sea)	Fish workers	OA?	HP

OA - Occupational Asthma

COPD - Chronic Obstructive Pulmonary Diseases (Bronchial Irritation and/or Non-Specific Airways Obstruction)

HP - Hypersensitivity Pneumonitis/EAA

Continuous dermal exposure to these materials is also likely to occur under working conditions. Dusts of various kinds settle out and tend to stick to sweaty skin where they may cause various inflammatory or allergic responses. Innoculation may occur through minor wounds.

Most symptoms and diseases appear to be dose dependent; thus, the amount of material per unit volume, the increased pulmonary ventilation required by metabolic needs and physical work, the duration of exposure, and individual susceptibility enter into any expression of risk. Where allergenic reactions are suspected, the risk to atopic individuals is especially difficult to characterize.

Area sampling combined with detailed job descriptions can provide estimates of individual exposure but personal sampling may be necessary for a more precise determination. Cumulative exposure estimates can be derived from work histories combined with historical environmental data or by assuming that past exposures were similar to present day exposures. Unfortunately, these estimates are often only crude approximations of actual exposures.

The length of the sample period is important in accurately determining exposure. Sample types include full shift, partial shift, and grab samples. In general, the full shift sample is the most accurate sample. Another consideration is the accuracy and reliability of the selected sampling and analytical methods. A good treatment of the systematic and random errors encountered in industrial hygiene sampling and analysis can be found in the NIOSH Occupational Exposure Sampling Strategy Manual (1977) and in Chapter 3

of Patty's Theory and Rationale of Industrial Hygiene Practice (1979).

Since the physical, chemical, and biologic nature of the agent of interest may be important factors in determining its effect, different types ~~of samples may be needed to fully characterize a single workplace. The choice~~ of a collection system for environmental assessment of worker's exposure is primarily determined by the physio-chemical nature of dusts and by their expected concentrations in air. The best single source of information on the different types of collection systems is probably the ACGIH's Air Sampling Instruments for Evaluation of Atmospheric Contaminants (1983). In addition, the book contains chapters on general industrial hygiene, filter selection, data reduction of particle size analyses, instrument calibration, and the sampling of microorganisms and airborne allergens.

In the following sections, information is presented on the available methods which may be used to sample and characterize organic dusts

#### 5.2.2 Sampling Appraisal

Once the presence of an occupational disease is established, the next step is to characterize the exposure-response relationship to determine an acceptable level of exposure. To accurately characterize the exposure, sampling methods must be selected that have size selection (sizing) or collection characteristics similar to the region of the human respiratory tract that is the primary site of action for the dust. Table 2 presents various sampling techniques that may be employed to collect vegetable dust.

**Table 2 - Occupational Sampling Methods for Non-byssinotic Vegetable Dusts**

<b>Exposure</b>	<b>Occupations</b>	<b>Sampling Method</b>	<b>Controls</b>
<b>1. Grain Dust Grain handlers</b>	<b>Grain elevator workers</b>	<b>Andersen viable sampler or AGI-30 (M)* High volume sampler (TD)* Personal sampler (TD/RD)* Pesticide** Andersen or Marple impactor (SS)* Gases (NO<sub>2</sub>, CO<sub>2</sub>, etc.)**</b>	<b>LEV*** R</b>
<b>2. Wood dust</b>	<b>Lumber and wood workers Board makers Timber and saw mill workers (Maple bark stripper's disease) Redwood workers (Sequoiolosis)</b>	<b>Personal sampler (TD) High volume sampler (TD) Andersen or Marple impactor Andersen viable sampler or AGI-30(M)</b>	<b>LEV R</b>
<b>3. Hay dust</b>	<b>Farmers (Farmers' lung)</b>	<b>Andersen viable sampler or AGI-30(M)</b>	<b>R</b>
<b>4. Rice dust</b>	<b>Farm workers (Millers and handlers)</b>	<b>Andersen viable sampler or AGI-30 (M)* High volume sampler (TD)* Personal sampler (TD/RD)* Pesticide** Andersen or Marple impactor (SS)* Gases (NO<sub>2</sub>, CO<sub>2</sub>, etc.)**</b>	<b>LEV R</b>

<sup>1</sup>Prepared by Nordman, H. & Finklea, J.F. for the chapter on "Prevention and Control."

Exposure	Occupations	Sampling Method	Controls
5. Tea dust (Black, Herbal, Green, Yellow)	Tea processors, Blenders and packers	Andersen viable sampler or AGI-30 (M)* High volume sampler (TD)* Personal sampler (TD/RD)* Pesticide** Andersen or Marple impactor (SS)* Gases (NO <sub>2</sub> , CO <sub>2</sub> , etc.)**	LEV R
6. Coffee dust (Green or Roasted)	Coffee processors, Blenders and packers	Personal sampler (TD/RD)	LEV R
7. Cocoa	Cocoa processors and packers	Personal sampler (TD/RD)	LEV R
8. Tobacco	Tobacco processors Cutters and blenders	Andersen viable sampler or AGI-30 (M)* High volume sampler (TD)* Personal sampler (TD/RD)* Pesticide** Andersen or Marple impactor (SS)* Gases (NO <sub>2</sub> , CO <sub>2</sub> , etc.)**	LEV R
9. Sugar cane dust	Sugar cane workers, Paper and board makers	Andersen viable sampler or AGI-30(M)	LEV R

<b>Exposure</b>	<b>Occupations</b>	<b>Sampling Method</b>	<b>Controls</b>
10. Kapok dust	Ginnery, bedding and Upholstery workers	Vertical elutriator (ID)* Andersen viable sampler or AGI-30(M)	LEV R
11. Coir (Coconut husk)	Brush and rope makers	Vertical elutriator (ID)* Andersen viable sampler or AGI-30(M)	LEV R
12. Natural resins and gums (Colophony, Acacia, Karaya)	Solders (Electronics) Printers and paper products manufacturers	Personal sampler (TD/RD)	LEV R
13. Castor bean, Flax, seed and cotton seed dust	Products of vegetable oil	Personal sampler (TD) High volume sampler (TD) Andersen or Marple impactor Andersen viable sampler or AGI-30(M)	LEV R
14. Orris Root and other vegetable dyes	Beauticians, cosme- tologists	Personal sampler (TD/RD)	R

<b>Exposure</b>	<b>Occupations</b>	<b>Sampling Method</b>	<b>Controls</b>
15. Tamarind seed	Weavers	Vertical elutriator (ID) Andersen viable sampler or AGI-30(M) Personal sampler (TD/RD)	LEV R
16. Paprika seed	Paprika stripping and Paprika grinding	Andersen viable sampler or AGI-30 (M)* High volume sampler (TD)* Personal sampler (TD/RD)* Andersen or Marple impactor (SS)*	LEV R
17. Chili	Grinders and handlers	Personal sampler (TD/RD)	LEV R
18. Mushroom dust	Mushroom workers	Andersen viable sampler or AGI-30(M)	LEV DV R
19. Malt dust	Brewery workers and Farm workers	Andersen viable sampler or AGI-30(M)	LEV R
20. Cork dust	Cork workers	Andersen viable sampler or AGI-30(M)	LEV R

<b>Exposure</b>	<b>Occupations</b>	<b>Sampling Method</b>	<b>Controls</b>
21. Pollens	Florists, Horticulturists	Rotorod, roto-slide, or other impactor	R
22. Proteolytic enzymes	Producers of food additives, detergent makers	Personal sampler (TD/RD)	LEV R
23. Tartrazine	Food processors	Personal sampler (TD/RD)	LEV R
24. Cheese mold dust	Cheese workers (Cheese worker's lung)	Andersen viable sampler or AGI-30(M)	LEV
25. Animal confinement	Animal Breeding (e.g. rodent handlers, lab. technicians) Bird handling (e.g. poultry pigeons, parrots, turkey, etc.)	Andersen viable sampler or ADI-30(M) High volume sampler (TD) Personal sampler (TD/RD) Andersen or Marple impactor (SS) Gases (NH <sub>3</sub> , H <sub>2</sub> S, CO, CH <sub>4</sub> , CO <sub>2</sub> , HCHO, etc.)	DV*** R
26. Feathers	Pluckers, sorters Bedding, etc. makers	Vertical elutriator (ID) Andersen viable sampler or AGI-30(M) Personal sampler (TD/RD)	LEV R

<b>Exposure</b>	<b>Occupations</b>	<b>Sampling Method</b>	<b>Controls</b>
27. Hoja (invertebrate) from sea)	Fish workers	Andersen viable sampler or AGI-30(M) Personal sampler (TD/RD)	R
28. Building Associated Hypersensitivity Pneumonitis and Humidifier Fever	Office workers	Andersen viable sampler or AGI-30(M) Personal sampler (TD/RD)	DV
29. Building Associated Asthma	Office workers	Rotorod, roto-slide, or other impactor Andersen viable sampler or AGI-30(M) Personal sampler (TD/RD)	DV
30. Pyrethrum		Personal sampler (TD)** High volume sampler (TD)**	LEV R
31. Jute and hemp	Jute and hemp workers	Vertical elutriator (ID) Andersen viable sampler or AGI-30(M) Personal sampler (TD/RD)	LEV R If possible, use chemical retting.
32. Cotton, flax	Textile workers	Vertical elutriator (ID) Personal sampler (TD/RD)	LEV DV

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\*(M) = Microbe collection  
(TD) = Total Dust Collection  
(RD) = Respirable Dust Collection (with cyclone)  
(SS) = Size Selection  
(ID) = Inhalable Dust Collection  
\*\*Sampling method depends upon specific compound  
\*\*\*LEV = Local Exhaust Ventilation  
R = Respirator  
DV = Dilution Ventilation

Particulates.

(i) Particulate Sizing. Recommendations for particle size-selective sampling have been outlined by Phalen and coworkers (1986). The reader is directed to this resource for a comprehensive review of the subject.

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The most common methods for determining the aerodynamic particle size distribution of workplace particulates (aerosols) utilize the inertial impaction theory. As an airstream passes through a small orifice it increases in velocity. Once through the orifice the airstream spreads out and its velocity decreases. Due to the inertia developed while being accelerated through the orifice particles tend to impact on the filter or plate below the orifice, rather than follow the airstream. The probability of a particle impacting is related to the aerodynamic size of the particle (which takes into account size, shape, and particle density), the size of the orifice, and the sampling rate. A cascade impactor has a series of these orifices and collection surfaces. Each lower stage has smaller orifices so that the air velocity through the orifices increases, which increases the impaction efficiency for smaller particles at each succeeding stage. Since each collection surface is pre- and post-weighed the percentage of the total mass of the aerosol captured by a particular stage can be determined. When these data, expressed as cumulative percentages, are plotted, using log-probability paper, against the aerodynamic equivalent diameter cutpoints for each stage the mass median aerodynamic diameter (MMAD) can be determined (ACGIH, 1983 & AIHA, 1986). The MMAD is felt to be the best parameter of an aerosol distribution for predicting the most probable site of deposition and biologic action (TGLD, 1966).

The primary advantage of the impaction methods is the separation and classification of particles by their aerodynamic diameter which is an accurate predictor of their probable site of deposition in the human respiratory tract.

Most cascade impactors operate at 28.3 l/m and require an externally powered vacuum pump. Airflow is regulated with a critical orifice. Most cascade impactors yield particle size data well into the submicron range. Recently two impactors have become available that can be operated with a battery-powered personal sampling pump. One is specifically designed to be worn by a worker and operated at 2 LPM (Sierra Instruments/ Series 290, 1983; Rubow, et al., 1987). The other can be operated over the range of 0.3 to 20 l/m although flowrates less than 3 l/m are recommended when using personal sampling pumps (Sierra Instruments/Series 260, 1983). Different size cutoffs for each stage can be calculated at different flowrates using a special circular slide rule provided by the manufacturer. With most impactors, particles larger than 10  $\mu\text{m}$  impact on the first stage but using the flexibility of this impactor the flowrate can be reduced to determine the size distribution of particles larger than 10  $\mu\text{m}$ .

Another recent development is that of a small, plastic impactor that is light, inexpensive, and designed to operate with a personal sampling pump calibrated at 2 l/m (Jones et al., 1983). To date, however, this impactor is not commercially available but is easily constructed using standard plastic 37 mm filter cassette bodies.

When sampling with an impactor, consideration should be given to the

expected size range of the aerosol. Large particles can cause particle bounce and re-entrainment, and may plug the impactor orifices (Anderson Samplers, Inc., 1983). These particles can be removed with an impactor preseparator, available for most cascade impactors. The mass of the particulate collected by the preseparator is added to that of the first stage when determining the particle size distribution from the impactor data.

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There are numerous electronic, direct readout instruments that can give mass concentration or particle size distribution data, but in general, these instruments are designed for laboratory use and most are not suitable for field applications. In addition, many respond to narrow particle size ranges or do not present data by aerodynamic diameter. These instruments are described in chapter U of ACGIH's Air Sampling Instruments for Evaluation of Atmospheric Contaminants (1983). A recently developed portable instrument not included in this book that uses light-scattering to determine both size distribution and mass concentration has been described elsewhere (PPM, Inc., 1983b).

(ii) Particulate Exposure Characterization. Three types of aerosol measurements have been used to characterize agricultural dusts or particulates: total dust, respirable dust, and inhalable dust. Total dust roughly correlates to that fraction of the aerosol that is capable of entering the human respiratory tract through either the nose or the mouth. It is now considered more appropriate to refer to this fraction as "inspirable dust" or the "inspirable fraction" (ACGIH, 1984). Respirable dust refers to that fraction that is capable of penetrating the lung into the alveolar regions.

Inhalable dust (also referred to as the thoracic fraction (ACGIH, 1984) and as lint-free respirable dust in the U.S. cotton dust standard) refers to that fraction that is capable of both alveolar and tracheobronchial deposition (Miller et al, 1979; NIOSH, 1975). A report by the ACGIH Air Sampling Procedures Committee (1984) gives a summary of and recommendations for size selective sampling to characterize particulate deposition in the various regions of the lung.

Actual regional deposition for any one individual will vary according to respiratory tract geometry, nasal versus pharyngeal inspiration, tidal volume, and inspiration rate. One study has shown that particles as large as 60  $\mu\text{m}$  in aerodynamic diameter can be inspired (Ogden & Birkett, 1977). Extrapolation of this work indicates that the inspirable size range may extend to particles as large as 185  $\mu\text{m}$  in aerodynamic diameter (ISO, 1983). A later study showed that particles as large as 130  $\mu\text{m}$  are inspirable (Vincent & Mark, 1982). The plastic filter cassettes used in dust sampling do not actually measure "total dust" per se, but are themselves size selective with lower collection efficiencies at the larger particle sizes (Agarwal & Liu, 1980; ACGIH, 1983). Recently, recommendations have been made that "total dust" sampling devices be designed to collect "inspirable" dust (ACGIH, 1984). The 37 mm plastic cassette with a 4 mm inlet at flowrates of 1 to 2 liters per minute corresponds to the tentative criteria suggested and can be considered an acceptable measure of inspirable dust. Vegetable and wood dust usually contain large, inspirable particles that may not be collected by a total dust sampling cassette. This is important only if nasopharyngeal deposition is considered relevant.

"Respirable dust" includes particles smaller than 10  $\mu\text{m}$  with a 50% cut-point at either 3.5  $\mu\text{m}$  or 5  $\mu\text{m}$  according to the American Conference of Governmental Industrial Hygienists (ACGIH) and the British Medical Research Council (BMRC) alveolar deposition curves, respectively (ACGIH, 1983).

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Preseparator devices can be used to remove the larger non-respirable particles from the sample airstream prior to collection. The percent of particles less than 10  $\mu\text{m}$  passing the preseparator roughly corresponds to the particle deposition characteristics of the alveolar region. Respirable dust sampling methods always utilize some form of preseparator in front of the collecting filter.

As applied to cotton dust, the term "inhalable dust" was used to refer to particles capable of both tracheobronchial and alveolar deposition. Inhalable dust has been used as a measure of fibrous vegetable dust such as cotton, flax, jute, hemp, and kapok. This measure of dust may have applicability in situations of byssinotic-like symptoms or where both alveolar and tracheobronchial deposition is of concern. Inhalable dust has been defined as having a 50% cut-point at 15  $\mu\text{m}$  (Miller et al., 1979). An alternative definition with a 50% cut-point at 10  $\mu\text{m}$  has been suggested by both the International Standards Organization (ISO, 1983) and the American Conference of Governmental Industrial Hygienists (ACGIH, 1984)..

Total particulates can be measured by a common gravimetric method which utilizes a filter mounted inside a plastic cassette and a rechargeable battery-powered sampling pump calibrated between 1.5 and 4 l/m. Such a system is portable and rugged. Due to its light weight, this system may be worn by a

worker to obtain a personal sample that accurately reflects his exposure. Such a unit may also be used to sample near a source of dust generation or as a general area sampler. Area sample data may be combined with time-motion data to determine worker exposures, although in general this provides a less satisfactory estimate of exposure than does personal sampling.

A high-volume sampler or a high-efficiency industrial vacuum cleaner can be used if gram quantities of airborne dust are required for chemical analysis. High volume samplers are available that can collect up to 1700 l/m through a 4 inch (10.16 cm) circular filter or an 8 x 10 inch (20.32 x 25.4 cm<sup>2</sup>) filter (ACGIH, 1983). Such units generally require an external power source. If placed near a dust generation source large non-inspirable particles may settle out onto the filter or they may be mechanically ejected from the source and captured by the high volume sampler. Such large particles may not be representative of the inspirable fraction of the dust; therefore, specially designed inlets should be used to prevent their collection.

Industrial vacuum cleaners are often used to collect large quantities of settled dust for analysis. One method which eliminates the need to clean the vacuum canister between samples is to attach a 37 mm filter and cassette to the vacuum nozzle and use the vacuum to fill the cassette with settled dust. Due to the possibility of static accumulation and the use of non-explosion proof motors, caution should be exercised when using a vacuum cleaner to collect vegetable dust capable of dust explosions (i.e., grain or flour dust).

Respirable particulate sampling differs from total particulate sampling

only by the addition of a particle preseparator prior to the filter. A commonly used preseparator is the 10 mm nylon cyclone. This device utilizes centrifugal force to separate and remove large particles from the air stream thus allowing only the respirable particles (i.e., those capable of penetrating to the alveoli) to pass to the filter. The collection

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~~characteristics of this sampling unit (filter preceded by a cyclone)~~  
reasonably correspond to that of the alveolar region when collected at 1.7 l/m. The combination of cyclone, filter and cassette, and personal sampling pump may be used for both personal and area monitoring.

Large quantities of respirable particulates can be collected using high volume cyclones. The sampling rates range between 9 and 240 l/m, depending on the size of the cyclone (ACGIH, 1983). A sampling pump requiring an external power source is required.

Other instruments for sampling respirable dust (mass) include the electrostatic precipitator, the horizontal elutriator, and several direct reading instruments. The horizontal elutriator is not suitable for personal sampling and traditionally has been used to characterize mineral dust exposures (Hinds, 1982). Several portable, direct reading instruments are available that use either a 10 mm cyclone or a single stage impactor to remove non-respirable particulates from the sampled air stream. Their principles of operation involve either beta-attenuation or the frequency change of an oscillating quartz crystal when loaded with collected particulate. There are numerous portable instruments that rely on light-scattering to measure respirable dust. These instruments are comprehensively described in Section U

of the ACGIH's Air Sampling Instruments for the Evaluation of Atmospheric Contaminants (1983). An instrument that utilizes the light scattering properties of particulates to determine respirable dust concentrations has been recently described (PPM, Inc., 1983a). Direct reading instruments are useful in determining areas of high concentrations as well as instantaneous concentrations but they are not suitable for accurately determining personal exposure.

Inhalable particulates are routinely sampled with a vertical elutriator or "VE" (Lynch, 1970), the instrument of choice for this methods application. The VE is specifically used in the United States to sample "lint-free respirable cotton dust" ("respirable" is defined in the U.S. cotton dust standard as including tracheobronchial deposition in addition to alveolar) (NIOSH, 1975). The VE has also been used to monitor exposures to other vegetable dusts. It was designed to collect particles capable of tracheobronchial and alveolar deposition when operated at a flowrate of  $7.4 \pm 0.2$  l/minute (NIOSH, 1975). The collection characteristics of the cotton dust VE have been described as including either a 50% cut-point at 15  $\mu\text{m}$  or a 100% cut-point at 15  $\mu\text{m}$  (ACGIH, 1983; NIOSH, 1975). Actual measurements place the cut-point at either 10.5 or 12  $\mu\text{m}$  with fractional collection of particles as large as 30  $\mu\text{m}$  (Rubow & Marple, 1983; Claassen, 1981). In principle, the VE excludes particulates (lint, etc.) having a settling velocity greater than the upward velocity of the airflow inside the elutriator body. The smaller particles are carried to the top of the elutriator to be captured by a tared 37 mm PVC filter mounted in an open-face cassette. A non-pulsating rotary pump requiring external power provides the 7.4 l/m flow rate (NIOSH, 1975).

A calibrated critical orifice is generally used to regulate the flow rate. This type of sampling device is large and bulky and is not suitable for personal sampling. Smaller, battery-powered vertical elutriators have been designed for cotton dust monitoring. Recently available is a portable instrument that uses light-scattering and a vertical elutriator preseparator to give inhalable dust data equivalent to the standard VE (PPM, Inc., 1983b). This instrument requires line voltage but allows real-time determinations of inhalable dust exposures.

Exposure to inhalable dust, such as cotton dust, is determined by stationing a suitable number of vertical elutriators in representative areas and by keeping a detailed time-motion study of the workers. No personal samplers are available that give results that correspond to those of the VE. Observations over the years indicate that a substantial fraction of the non-respirable lint does penetrate to the filter. This phenomena has been verified using monodisperse aerosols as large as 30  $\mu\text{m}$  in aerodynamic diameter and has been ascribed to the high centerline velocity of the VE (Claassen, 1979; Claassen, 1981). In summary, the VE does not provide a sharp cutoff at 15  $\mu\text{m}$  and may collect particles (lint, etc.) considerably larger but it is widely used and a great deal of exposure-response data have been developed using VE exposure data.

#### Microbiologicals.

Most of the methods used today to monitor airborne fungi and bacteria were developed from industrial hygiene sampling methods traditionally applied

to characterize inorganic dusts. Microbial sampling is more complicated than dust sampling in that there are no "accepted" techniques and little or nothing in the way of recommended exposure standards.

Typically, microbiological sampling involves the collection of bacteria or fungi onto appropriate agar media. The media is incubated at an appropriate temperature and the number of colonies counted. Knowledge of the volume sampled allows a determination of the concentration of airborne microbes. Table 3 lists the most frequently used samplers.

Enumeration of bacteria and fungi requires specific growth media. Bacteria are usually incubated using a broad spectrum media such as tryptic soy agar. If heavy fungal contamination is expected, a fungal inhibitor, such as cycloheximide, should be added to the media. Fungi are usually incubated using a broad spectrum media to which penicillin or streptomycin has been added. A recent comparison of fungal media recommends Rose Bengal-Streptomycin Agar as a good broad spectrum media (Morring et al., 1983). Thermophilic bacteria, such as *Micropolyspora* or the *Thermoactinomyces* spp., can be differentiated from mesophilic bacteria by incubation at 50-55°C rather than 35°C.

The most common sampling techniques use midget impingers, liquid bubblers, microbial cascade impactors, rotating slit (slit-to-agar) samplers, membrane filters, or open petri dishes. Results are given in either total organisms per cubic meter when using liquid samplers or colony forming units (CFU) per cubic meter when using impaction techniques.

Table 3 - Samplers Most Frequently Recommended for Use in Sampling Microbial Aerosols

Sampler	Principle	Sampling Rate ppm	Sampling Time	Application
Andersen multistage sieve-type (A, 1)	Impact on nutrients	28.31	1 min Min. (*) 20 min Max.	Bacteria and viruses.
Andersen 2-stage disposable sieve-type	Impage on nutrients	14-28.3	1 min Min. (*) 20 min Max.	Low to medium concentration aerosols, collects CFU unless surfaces are washed into medium. Provides particle-size data.
AGI-30 raised jet all-glass impinger (A, 2)	Impinge into fluid	12.5	ca. 15-60 min Max.	Bacteria, viruses etc. it works on wide range of concentrations.
Large volume electrostatic (LVS/2K) (LVS/10K) (3)	Combination electro- and impaction into fluid	500 to 10 000	Unlimited. (fluid may be recirculated with some makeup)	Bacteria & viruses. Collects into fluids & counts total viable unit. Efficiency 80-95% of AGI-30.
Membrane filter (5)	-	5-50	"minutes" for bacteria & virus longer for spores & fungi	Primarily hardy spores but can be used for bacteria and viruses.
Slit sampler (6)(7)	Impaction	28.3	1 min to 1 hr	Provides time-concentration. Collects CFU. Limited concentration range.
Open Petri dish with nutrient agar	-	-	0-4 hrs (*)	Biased to collect large particles (CFU).
Open settling surface uncoated	-	-	Unlimited	Same as above, collects hardy spores.
Hirst spore trap (7)	Impaction	10	24 hrs.	Spores and pollen collected outdoor.
Multistage liquid impinger (8)	Impingement	55	varies	Collects individual cells gently at moderate flow rates with size selection similar to respiratory tree.

(\*) May be extended by use of oxyethelene docosanol wash. (See May, 1969)

(A) Recommended as "laboratory standard" samplers.

(1) Andersen 2000 Inc. P.O. Box 20769, Atlanta, Georgia 30320, USA.

(2) Ace Glass, Inc., Vineland, New Jersey 08360, USA.

(3) Litton Systems, Inc., Applied Science Division, 2003 East Hennepin Ave., Minneapolis, Minnesota, 55413, USA.

(4) Sierra Instruments, Inc. P.O. Box 909, Carmel Valley, California 93924, USA.

(5) Gelman Instrument Co., 600 South Wagner Road, Ann Arbor, Mich. 48106; Millipore Filter Corp., Bedford, Massachusetts 01730, USA.

(6) New Brunswick Scientific Co., Inc., 1130 Somerset St., New Brunswick, New Jersey 08903, USA.

(7) C.F. Casella & Co., Ltd., Regent House, Britannia Walk, London W. 1, England.

(8) A.W. Dixon & Co., 30 Anerly Station Road, London S.E. 20, England; BGI Inc. 58 Guinan St., Waltham Massachusetts 08154, USA.

Sample duration varies with the method but generally is less than one hour. Multiple samples are thus required to obtain a full-shift exposure. If high concentrations are expected, the sample duration should be reduced accordingly. Extended sampling periods are not desirable due to the possible reduced viability of microorganisms collected early in the sample period (ACGIH, 1983).

Impingers (all glass impingers) are often used even though this method requires the additional steps of serial dilution and plating onto agar plates. The evaporation of liquid during sampling is a further disadvantage (Wolf et al., 1959). Liquid impingement tends to break up particle aggregates, thus the results are best expressed in total organisms per cubic meter. A standard impinger for microbial sampling is the AGI-30 (available from Ace Glass, Inc., Vineland, NJ 08360, U.S.A.; item number 7540-10). This impinger is operated at 12.5 l/m.

Another often used instrument is the high volume liquid scrubber which relies upon electrostatic precipitation to collect the particulate. Due to its high sample rate (400 to 1000 l/m) this instrument is useful where the particulate concentrations are low (ACGIH, 1983).

Membrane filters may be used but require additional treatment after sampling in order to quantitate the captured organisms. In addition, the dessication effect of air moving through the filter limits the use of filters to fungal spores and only the most hardy of bacterial spores (ACGIH, 1983).

The open petri dish (settling plate) method has traditionally been used to give a relative measure of airborne microorganisms but it is not possible, using this method, to calculate exposure in CFU/m<sup>3</sup>. Disadvantages also include preferential collection of large particles (due to their greater settling velocity) and lack of reproducibility. Samples collected by settling are comparable only if the environmental conditions (air velocity and direction) are held constant, something not often found in occupational settings.

Slit samplers can be used to determine the average concentration in CFU/m<sup>3</sup> during the sample period and the concentration for any given time period during the sampling cycle. This provides the user with a means to examine the effect of process changes or work habits on the airborne microbial concentrations. The principle of operation involves rotating a petri dish, containing selective media, under a slit through which air is drawn at a sampling rate of up to 50 LPM. A vacuum pump and power source are required (ACGIH, 1983).

The impaction methods are simple and appear to be the most field-rugged. Most of the microbial impactors operate at 28.3 l/m and require a vacuum pump and a power source. Six-stage cascade impactors are available that are designed to accommodate nutrient filled petri dishes. The surface of the agar serves as the impaction surface. Each stage contains up to 400 orifices and the spores tend to impact and grow into colonies in the pattern of the jets. After incubation, total colony forming units are determined by summing the colonies from each of the six stages and dividing by the total volume of air

sampled . Since each stage captures particles of a certain size range the respirable and non-respirable CFU/m<sup>3</sup> can be determined. The primary disadvantage of this sampler is the possibility of more than one spore landing at the same point on the agar surface. This results in a bias towards low colony counts which can be minimized by counting under magnification or by using a statistical procedure developed to eliminate this bias (Anderson, 1958).

Two-stage and single-stage impactor options are available. The two-stage microbial cascade impactor separates the particles into respirable and non-respirable categories and is commercially available in either a metal or a plastic disposable version. It can also be easily constructed by removing four stages from a 6-stage model. The two-stage model may underestimate the CFUs when compared to the 6-stage model (Gillespie et al., 1981).

The other option involves a modification in the use of a 6-stage microbial impactor. This sampler, called the N-6, uses either of the last two stages and one petri dish. Results of the single stage microbial sampler slightly overestimates the microbe concentrations when compared to the 6-stage configuration (Jones, et al., 1985).

The advantage of the two and single stage impactors resides in the lower number of plates to be handled and enumerated and the lower sample times required. Disadvantages include a small loss of accuracy when compared to the 6-stage viable impactor, the absence of particle size data (for single stage), and an inability to handle large concentrations unless the concentration is

estimated beforehand and the sampling time adjusted accordingly. Since particle size data on viable aerosols may not be medically useful information in many situations, the single stage samplers with their lower support requirements represent a strong alternative to the 6-stage sampler.

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~~Since the desired fraction of the microbial aerosol consists of living~~ organisms, it can be argued that nearly every sampling method stresses the organisms in one way or another resulting in a certain amount of organism mortality. Thus, it may be impossible to collect, culture, and enumerate every viable organism in an aerosol. In the absence of a standard method for sampling microorganisms, sampling methods should be chosen that are capable of yielding reproducible data on the "relative" concentration of airborne organisms. However, Brachman et al. (1964), recommended either the AGI-30 impinger or the 6-stage microbial impactor as standard methods. The ACGIH Bioaerosols Committee develops microbial sampling protocols for different environments, including agricultural, and has recommended the N-6 method for office environments (ACGIH, 1986).

#### Gases and Vapors.

Often in animal confinement the gaseous products of anaerobic fermentation of organic material - ammonia, methane, hydrogen sulfide, and carbon dioxide - are of concern to the investigator. Where flame heating units are used in cooler weather, carbon monoxide may be an additional concern. Nitrogen dioxide has been found where green vegetable matter is confined in silos.

Ammonia, carbon dioxide, hydrogen sulfide, and nitrogen dioxide are most commonly monitored using either direct reading indicator tubes or direct reading instruments specifically designed for each gas. Since methane is a simple asphyxiant, the concern is for percentage quantities that reduce the relative concentration of oxygen. Therefore the combustible gas indicator (CGI) is most often used for methane monitoring. The CGI reads in percent of the lower explosive limit (% LEL) which may be converted to parts per million. If excessive levels of methane or carbon dioxide are suspected, the oxygen content should also be monitored with a direct reading oxygen meter (ACGIH, 1983; NIOSH, 1973).

Passive dosimeters are available for hydrogen sulfide, ammonia, carbon monoxide, and nitrogen dioxide. The hydrogen sulfide and ammonia dosimeters are analyzed after sampling but generally the support instrumentation is neither excessively expensive nor complicated. The carbon monoxide dosimeter is direct reading. Dosimeters for nitrogen dioxide are either direct reading or must be analyzed colorimetrically after sampling. Passive samplers can provide a full shift sample unlike the above direct reading instruments and indicator tubes. Section S of ACGIH's Air Sampling Instruments for Evaluation of Atmospheric Contaminants (1983) contains a good review of passive samplers and the available devices.

Long term (full shift) indicator tubes are available for ammonia, carbon monoxide, carbon dioxide, and hydrogen sulfide. These tubes require a special low flow sampling pump that may be attached to a worker but have the advantage of direct reading at the end of the sampling period.

If the appropriate sampling equipment - personal sampling pumps and midget bubblers or impingers - is available along with the appropriate laboratory support, more accurate methods such as those published by NIOSH (1984) may be used.

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### Calibration.

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All sampling pumps require periodic calibration to insure that they are operating at the desired flowrate. The most common methods for calibrating the battery-operated personal sampling pumps use bubble meters, wet test meters, or calibrated rotameters. Also available are electronic mass flow measuring devices that are useful when calibrating a large number of pumps. These should also be calibrated against a primary standard such as a bubble meter. High volume sampling devices may be calibrated with a dry gas meter; however, accurate calibration is often not necessary if they are used only to collect large quantities of particulates for chemical analysis. A review of calibration methods can be found in various references (ACGIH, 1983; NIOSH, 1973; Patty, 1978).

#### 5.2.3 Analytical Appraisal

An accurate and reliable analytical appraisal of the airborne dust is essential for recognition and evaluation of the hazard potential and for subsequent control. Sample analysis can be categorized as either gravimetric, microscopic, chemical, biological or physical. In order to understand the type of sample analysis that should be done, it is necessary to understand the

following four criteria:

- o The nature of the hazard, including route of entry into the body and site of action in the body;
- o The process which generated the hazard and the expected contaminant levels;
- o The limitations on sampling, since certain kinds of sampling equipment may be unsuitable for a given situation; and
- o The cost and availability of the analytical equipment, since more sensitive techniques are generally more costly and more difficult to perform.

Quality control of the analytical procedures is the only way to assure the reliability of the analysis itself. Blank samples treated in the same manner as the actual samples but unused and positive control samples prepared with a known amount of contaminant are useful in maintaining quality control. Generally, one blank sample should be included at least for every ten samples that are taken. The positive controls should include a sample concentration near the mean of the samples being analyzed, if possible. Accurate calibration of both sampling and analytical equipment is necessary as well, as has been discussed.

#### Gravimetric.

Selection of the proper filter is an important step in selecting a sampling method. Filters vary in dimension, composition, pore size, air flow

resistance, and collection efficiency. Filters are made of cellulose ester, glass fibers, polycarbonate, polyvinyl chloride (PVC), or polytetrafluoroethylene. Non-hygroscopic polymeric filters are best for gravimetric analysis. These are generally the polycarbonate and polyvinyl chloride filters. Some filters use organic binders and are not suitable for ~~the analysis of certain chemicals.~~ The 37 mm diameter filters and plastic cassettes are widely used for personal sampling. These filters typically have a pore size of 0.8 or 5  $\mu\text{m}$ . In general, filters with a 5  $\mu\text{m}$  pore size provide high collection efficiencies even for submicron particles and are suitable for most sampling applications.

An essential part of gravimetric sampling is the weighing of filters before and after sampling. It was once believed that filters should be dessicated prior to each weighing. Recent work indicates that a filter will regain the major fraction of the moisture lost during dessication within 60 seconds of being removed from the dessication chamber, rendering the dessication procedure nearly useless (Hawley & Charell, 1980; Charell & Hawley, 1981). Moisture adsorption is most pronounced with the cellulose ester filters, but even the "non-hygroscopic" polymeric PVC and polycarbonate filters exhibit appreciable weight gains after removal from a dessicator. Therefore, for best results, especially where small particulate gains are expected, all weighing should be done in an environment where the "absolute humidity" (both humidity and temperature) is controlled (Hawley & Charell, 1980; Charell & Hawley, 1981). Such conditions may be created in an environmentally controlled room or in the mini-environment of a glove box. When polymeric filters are used and moderate to large weight gains are

expected (greater than 1 mg of collected mass), errors due to moisture effects are small and such strict attention to controlling moisture gains is not necessary.

For best results filters should be weighed on an analytical electrobalance (microbalance) capable of resolving to 0.01 milligrams. The 37 mm filters typically weigh between 10 and 35 milligrams, depending on composition. High volume filters, which weigh approximately 3 grams, require a semi-micro balance capable of resolving to 0.1 milligrams. Electrobalances require a steady power supply; therefore in areas where the voltage varies, a quality mechanical balance capable of resolving to 0.1 milligrams may be a better choice. With any balance, attention should be given to proper maintenance, calibration, and the provision of a firm, vibration-free surface for the weighing of filters. Both pre- and post- weighings should be done on the same balance by the same technician. If the mass gains are expected to exceed 1 milligram, the semi-micro mechanical balance is sufficiently sensitive for filter weighing.

#### Microscopic.

Prior to the advent of the inertial impaction methods, dusts were sized using the light microscope and a Filar micrometer or Porton reticle. This method is still widely used where impactors are not available. Samples can be collected using either the midget impinger or a cellulose ester membrane filter, mounted in an open-face cassette. Liquid samples are first transferred to a Dunn cell or haemocytometer before particle sizing using the

light microscope. Membrane filters need only be rendered transparent using acetone vapor (NIOSH, 1984) or a 1:1 solution of dimethyl phthalate and diethyl oxalate. In both cases the particles are best sized with a Porton reticle using the particle's "projected area" (NIOSH, 1973). Optical sizing is time consuming, tedious, and does not yield data on the aerodynamic diameter of the particles. ~~If the density of the material is known a rough estimate of the aerodynamic diameter may be obtained. If the material is fibrous, it is difficult to predict the site of deposition from optical sizing data. In general, the data derived from optical sizing is less useful than impaction data in predicting the probable sites of respiratory tract deposition.~~

#### Chemical.

Glass fiber filters are often used for high volume sampling and where the collected material will be chemically analyzed after sampling. (High volume filters are rated by efficiency rather than pore size for a given size range. Most high volume filters are 99.9% efficient for particles above 0.3  $\mu\text{m}$ .) Vegetable dust samples collected on filters can be analyzed for their carbohydrate and protein fractions - to differentiate between the organic and mineral fractions - and for the amount of gram-negative bacterial endotoxins.

It may be necessary to analyze the vegetable dust for toxic metals or pesticides and other chemicals. The methods of analysis can then involve expensive and sophisticated equipment. Table 4 lists most types of chemical analysis and the contaminants for which they are suited.

Table 4 - \*Analytical Techniques for Selected Occupational Contaminants

Method	Principle of Operation	Instrumentation	Sample(a)	Specificity(b)	Sensitivity(c)	Typical Applications
<b>Absorption Spectrophotometry</b>						
a. Visible	Measure of selective absorption of transmission of visible light, usually following reaction with a reagent that produces a color change.	Colorimeter; Spectrophotometer	SLG	Fair	0.005v ppm	Metals, NH <sub>3</sub> , phenol, SO <sub>2</sub> , NO <sub>x</sub> , oxidant gases (O <sub>3</sub> ), TOC (total organic carbon)
b. Ultraviolet	Absorption of ultraviolet light.	UV spectrophotometer	SLG	Fair	0.005 ppm	Organic compounds, some inorganic gases, e.g., SO <sub>2</sub> , O <sub>3</sub> , NO <sub>2</sub>
c. Infrared	Absorption of infrared radiation.	IR spectrophotometer	SLC	Fair	1 ppm	Organic compounds, some inorganic gases, e.g., CO, CO <sub>2</sub> , SO <sub>2</sub> , NO <sub>x</sub> , NH <sub>3</sub> , O <sub>3</sub> ; TOC
<b>Atomic Absorption Spectrophotometry</b>	Absorption of radiation by free atoms in a vapor state.	AA spectrometer	SL	Excellent	0.001 ppm	Most metals
<b>Emission Spectroscopy</b>						
a. Flame Photometry	Spectral-emission analysis following excitation by flame (arcs or sparks are also used).	Flame photometer; Spectrograph (arc)	SL	Good Excellent	0.001-0.1 ppm	Metals, halogens, phosphorus, sulfur (depending on specific method)
b. X-ray Fluorescence spectrometry	Spectral-emission analysis following x-ray excitation.	XRF spectrometer	SL	Good	10 ppm	All elements having atomic numbers above 11.
c. Spectrofluorimetry	Reemission of radiation absorbed by dissolved molecules.	Recording spectrofluorimeter	SL	Good	0.001 ppm	Organic compounds; some inorganic constituents
d. Chemiluminescence	Emission of spectral radiation resulting from a chemical reaction.	Chemiluminescence analyzer	G	Excellent	ppb	O <sub>3</sub> , NO <sub>x</sub>
<b>Mass Spectrometry</b>	Determination of material by creation of ionic current via electrostatic or electro-	Mass spectrometer	SLG	Excellent	ppb	Organic compounds

(\*Adapted from Lippmann & Schiesinger, 1979)

Table 4 (continued)

Method	Principle of Operation	Instrumentation	Sample <sup>(a)</sup>	Specificity <sup>(b)</sup>	Sensitivity <sup>(c)</sup>	Typical Applications
	magnetic field and separation of the ions according to their mass. Generally used in conjunction with gas chromatographs.					
Chromatography (gas; liquid; thin-layer)	Differential separation of agents due to selective retention in a fixed phase while subjected to movement by a flowing bulk phase.	Gas chromatograph, liquid chromatograph	LG(gas chr) SL(liquid chr) SL(thin-layer)	Excellent(gas) Good(liquid)	ppb-ppm	Organic compounds, trace metals, anions
Electrochemical a. Conductivity	Measurement of electrical conductivity following absorption of an agent through a solution.	Conductivity meter	LG	Poor	0.01 ppm	Any gas which forms electrolytes in aqueous solution, e.g. SO <sub>2</sub> , NO <sub>2</sub> , Cl <sub>2</sub> , H <sub>2</sub> S, NH <sub>3</sub>
b. Coulometry	Quantitative electrochemical conversion from one oxidation state to another.	Coulometer	L	Good	1 ppm	SO <sub>2</sub> , NO <sub>2</sub> , O <sub>3</sub> , H <sub>2</sub> S, aldehydes, F-, mercaptans
c. Polarography	Electrolysis of solution and measurement of current voltage relation.	Polarograph	L	Good	0.1 ppm	Some organic compounds and some metals, e.g., Sb, As, Cd, Cr, Ni, Zn
Neutron Activation Analysis	Measurement of emitted ionizing radiation following production of radionuclides by neutron bombardment.	-	SL	Excellent	ppb-ppm	Hg, As, Pb, Fe, and about 66 other elements which can become radioactive when bombarded with neutrons

<sup>a</sup> Sample: Most usual form of sample suited to the specific method; S-solid; L-liquid; G-gas.

<sup>b</sup> Specificity: This is an indication of the general ability of the method to measure the material in the presence of interferences.

<sup>c</sup> Sensitivity: The classifications are very broad and use of preconcentration or separation methods may increase specificity. Typical lower limits of detection are presented; these may differ depending upon the specific chemical analyzed and the background concentrations present.

Residual pesticides quite often remain on plant material as it is processed. Herbicides such as paraquat can affect the respiratory tract. Other pesticides have important systemic effects. NIOSH (1984) has published air sampling and analytical methods for paraquat and the more commonly encountered organophosphates, malathion and parathion, and halogenated hydrocarbon pesticides including aldrin, dieldrin, toxaphene, lindane, DDT, and others. These methods typically involve collection with a glass fiber filter, midget impinger, or both and analysis by gas chromatography or high pressure liquid chromatography.

Bulk samples are analyzed using techniques similar to those used for air samples, except that more effort may be required to clean the sample of extraneous matter. A good source for analytical techniques for herbicides and pesticides is EPA's Analytical Reference Standards and Supplemental Data for Pesticides and Other Organic Compounds (1981).

#### Biological.

There are no established limits for concentrations of airborne allergens and microorganisms. The use of samples must be in conjunction with cases where a particular disease etiology is suspected or where sampling is being done to quantify the effect of a particular control measure. The types of analysis that are done are enumeration of colonies for viable organisms, followed by speciation whenever possible and antigen testing of both viable and non-viable components of biological contaminants.

For enumeration and speciation, nutrient agar media is used to support growth of the viable organisms. The organisms may be collected directly onto plates containing the media in an impactor or transferred from water used in an impinger collection method. The nutrients and other ingredients of the agar will depend upon the type of organisms that are sought or thought to be present.

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Culture media must be checked both for sterility and the ability to support the growth of the organisms to be collected. Culture plates used for blank controls should accompany the plates used for sampling and be placed into the sampler with the flow off. Generally, contamination that occurs during the preparation of the plates can be detected by incubating all the plates at the appropriate temperature before they are used. Contaminated plates can then be disposed and the rest assumed to be sterile. Plates with obvious contamination after sampling (such as a streak of organisms where there should only be single points) should be discarded, as well. If more than one or two colonies are detected on the blank controls, the reason for the contamination should be determined and appropriate measures taken that include discarding the results of the sampling, if necessary.

#### Physical.

Analysis of the physical properties of contaminants largely pertain to the physical properties of particles. These properties determine the probability that a particle can penetrate to a site of biological action and also the effect the particle will have at the site of action. Since the major

site of action is the lung, the aerodynamic diameter is the most important physical property of a non-fibrous aerosol for predicting the site and probability of deposition in the lung. The collection method, if based on aerodynamic principles, serves as the method of analysis.

For particles depositing in the alveolar region, samplers are available which provide both personal and high-volume samples. For other regions of the lung, only high volume samplers are available. However, impactor samples can be used to estimate both the alveolar (respirable) and thoracic deposition. As seen in Table 5, both types of deposition can be determined from cascade impactor particle size data. Procedures for plotting and analyzing cascade impactor particle size data are readily available (ACGIH, 1983; AIHA, 1986; Hinds, 1982).

Finally, the electrostatic charge may affect both the site of deposition and the amount of material deposited in the lung. To determine the charge, by size, of an aerosol, an electrostatic elutriator, as described by Vincent, et al. (1983), can be used to obtain the charge distribution. Work done in a jute factory showed the amount of charge to be highly variable from factory to factory. It should be expected that most vegetable dust, by its nature, can be highly charged and difficult to collect with polymeric equipment.



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6. PREVENTION AND CONTROL<sup>1</sup>

The disorders dealt with in this report are highly variable. The only common denominators are that they are caused by inhaled dusts of vegetable or ~~other natural origin and that the respiratory tract is affected.~~ Whereas some of the offending agents merely cause nonspecific irritation, others result in a highly specific sensitization which in some instances is elicited by an immunological mechanism. Adding to the complexity is the fact that practically no data on dose-response relationships exist for sensitizing dusts or agents. Furthermore, vegetable and other organic dusts can also contain residues of a number of different pesticides. Pesticides stringently regulated or even banned in a country, because of perceived health rules, may be present in imported agricultural products.

Seasonal variations in crop production and the migratory nature of substantial numbers of the workforce complicate prevention and control efforts. Employees may work for long hours for a few weeks in one location, sometimes sustaining relatively high exposure for short periods of time. For these reasons, permissible exposure levels based upon an eight-hour workday or forty-hour workweek may not be appropriate. Prevention and control measures are less straightforward for these exposures than for dusts with well-known effects (e.g., coal, quartz, asbestos, and even cotton, flax, and hemp.) In short, details of preventive measures vary from industry to industry and should be planned and carried out separately for each situation. Some basic principles are, nevertheless, common for dusty workplaces; these are briefly outlined below.

Measures can be directed towards the work environment or the worker. Preventive measures, such as preemployment screening in search of susceptible individuals, must never be substituted for technical measures which aim at the reduction of exposure.

### 6.1 Identification of health risks

Ideally, a potential health risk should be predictable and protective measures should be introduced early in the planning stage of the occupational design in order to preclude exposure. Preventive measures are practical with known harmful substances or when the structure or characteristics of agents make such precautions desirable. More commonly the risk is identified after adverse effects occur in people already at work.

The first step in the identification of a hazard is usually clinical observation. Health personnel, employers, and employees should be alert to the possible associations between symptoms and exposures occurring in the work environment. Improvements in the education of health professionals, workers, and employers are needed to ensure that cases of occupational respiratory disease and potentially hazardous occupational exposures are recognized. The next steps after clinical observations are recorded, should be to verify the hazard and to assess its magnitude by competent reporting systems for occupational respiratory disease and epidemiological surveys.

Monitoring exposures in the work environment is a means of identifying potential risks before adverse effects have occurred. This measure is important in the prevention of irritant effects, whereas the usefulness of monitoring is limited with respect to sensitizing agents.

## 6.2 Engineering methods of dust control

The basic engineering methods of controlling dust are: the total enclosure or segregation of dusty processes; the use of water or wetting ~~agents to prevent particles from becoming airborne; the control of microbial~~ growth; and exhaust and dilution ventilation (Schilling, 1981; Grant, 1983). When new technology replaces traditional production processes, care should be taken to ensure that the appropriate environmental and engineering controls are an integral part of such technology transfer.

Total enclosure or segregation. The total enclosure or isolation of a process can reduce the risk of exposure to short periods of maintenance and repair, during which other protective measures can be used. For example, enclosure of conveying systems in grain elevators along with dust removal or appropriate ventilation to avoid explosive hazards would be an efficient way of reducing a dust problem (Conkey, 1980).

The principle of enclosure can likewise be used by providing a work station or clean environment for the worker to use when he is not required to be close to points of dust generation. For example control rooms, air curtains, or filtered-air booths can provide a means of reducing total exposure. Such applications have been successfully used in the grain elevator industry.

In situations where the evolution of dust cannot be prevented and the process cannot be enclosed, segregation may offer a means of reducing exposure. As a preventive measure, segregation has two major advantages. First, the number of exposed workers can be minimized to those necessary for

the process. Secondly, it may be easier to apply other measures of dust control if the dusty process is confined to one area. Although less efficient than total enclosure, segregation in combination with other control measures is recommended for many dusty types of work (e.g., the handling of moldy hay in a closed space).

Suppression of dust. Water and wetting agents can be used to suppress dust by keeping it moist. Wetting methods are used to prevent dust from becoming airborne. Airborne dust cannot easily be controlled by wetting methods, although sprays and high pressure waterjets have sometimes been successfully used for the suppression of inorganic dusts, for control of tea and coffee dusts, and in air conditioning, heating and ventilation systems.

Control of microbial growth. The extensive growth of various microorganisms and the resultant inhalation the spores causes hypersensitivity pneumonitis in a variety of occupations. Such conditions include bagassosis, malt workers lung, suberosis, and the most common of them all -- farmer's lung.

The active agents in hay dust which cause hypersensitivity pneumonitis are normally bacterial spores such as Micropolyspora faeni, Thermoactinomyces vulgaris, or spores of fungi belonging to the Aspergillus group. Prevention of the molding of hay is the obvious way to decrease the risk of contracting disease. This can be achieved in several ways, some of which are dealt with under other headings. Storage dryers are an efficient means of prevention. The addition of chemicals such as propionic acid to hay and straw has not been very successful (Lacey et al., 1978). The addition of such chemicals to the

substrate evenly enough to prevent molding is difficult. Moreover, some microbes are able to metabolize propionic acid and thus facilitate the growth of yet other microbes.

~~Humidity control in enclosed environments is required in various~~  
industrial processes such as printing. It has also become increasingly common to regulate humidity in offices and private residences (optimal relative humidity: 30% to 50%). For reasons of economy, air and water are often recirculated, especially in winter. Ventilation systems in air-conditioned buildings may also contain water sumps and pools of stagnant water. The water and organic dust drawn into the system may easily become contaminated by microorganisms, and microbial material may consequently be dispersed into the environment being ventilated. Exposure to such organic material may occasionally cause asthmatic attacks (Solomon, 1974), hypersensitivity pneumonitis (Banaszak et al., 1970), or humidifier syndrome (Nordman, 1984).

The most effective way to keep the water free of humidifier antigens is the introduction of steam in place of water. The addition of hydrogen peroxide or other oxidizing agents may be effective in controlling the growth of microorganisms, but may cause deterioration in the structure of the humidifier unit. The introduction of a biocide into contaminated humidifiers has proven ineffective and undesirable, as the chemical itself was dispersed into the environment (Pickering et al., 1976). However, the use of biocides in other instances, e.g., decontamination and maintenance of building ventilation systems may be useful.

Although the active component in cotton bracts and dust has not been isolated, treatment of raw cotton with gaseous hydrogen chloride or acetic

acid has previously been suggested as a method to inactivate the causative agents (Parkes, 1982). Current investigation (Castellan et al., 1984) of the acute bronchoconstriction induced by cotton dust suggests that the response is dose-related to airborne Gram-negative endotoxin concentrations. (For further discussion of byssinosis, see the WHO Report (1983) and Chapter 3 of the present publication.)

Ventilation. Ventilation systems should be constructed to meet specific needs, which vary with the degree of dust released and the characteristics of the dust. The main types of industrial ventilation are dilution ventilation and local exhaust ventilation. Dilution ventilation, or the removal (or supply) of air from a general area, room, or building for the purpose of comfort control, is predictable only within broad limits and therefore restricted to agents of low toxicity. Local exhaust ventilation captures the dust close to the releasing source and hence prevents the dust from entering workers' breathing zone. This specific characteristic makes it more suitable for the control of contaminants of high toxicity (Molyneux, 1981). The applicability of local exhaust ventilation is considered greater than that of dilution ventilation, as there is a wide range of hood designs which can be tailored to meet specific demands (e.g., ventilation built into soldering irons to prevent exposure to colophony).

Dilution ventilation diminishes the concentration of dust but does not guarantee that workers will breath clean air. Excessive dilution ventilation may even disturb dust and keep it airborne and may interfere with the correct functioning of local exhaust ventilation systems.

### 6.3 Substitution

One way to eliminate an occupational hazard is to substitute an innocuous substance, if feasible, for a harmful one. Substitution may itself involve health risks, or disruptive effects on producers of food and fiber, or even national economics. Thus, synthetic fibers have been used instead of the more detrimental natural fibers such as hemp and jute, and viscose fibers have been substituted for cotton. In the latter case, exposures of viscose workers to carbon disulfide have resulted in major health problems. A change in process, (e.g., substitution of chemical for biological retting) may reduce the toxicity of vegetable dusts.

### 6.4 Work practices

General cleanliness of the workplace is a simple means of achieving lower concentrations of dust. This aspect is frequently overlooked. Apart from reducing exposure, it always encourages orderliness and therefore safer work methods (Schilling, 1981). Dry brushing and the use of airblowing hoses is still common, although vacuum cleaning or hosing could easily be substituted. As far as allergenic dusts are concerned, vacuum cleaners are rarely equipped with proper filters, e.g., high efficiency particulate air filters; and so as a rule, allergens are blown out through the other end of the vacuum cleaner. Washing, using showers, and changing clothes when leaving work should be routine in all workplaces where harmful substances are present in the air.

### 6.5 Environmental monitoring

Recommended permissible exposure levels for workplace air can be found for a variety of harmful substances but only for a few organic dusts.

Recommendations vary from country to country, depending upon differences in concepts for setting such standards. Regardless of the concepts, monitoring concentrations in workplace air is necessary to insure standards or recommendations are met. The monitoring of environmental levels also serves the purpose of detecting disturbances in processes or dust control systems (Molyneux, 1981).

It should be emphasized that soundly based, permissible exposure levels for organic and vegetable dusts have not been established. In the past, vegetable dusts may have been looked upon as nuisance dusts. The sensitizing properties of dust have usually been neglected when permissible levels are set. With the exception of pharmaceuticals and pathogenic organisms, dusts originating from microbial growth have not received much attention by legislative or regulatory authorities, probably because of the paucity of data. The difficulties in setting permissible levels for sensitizing dusts are increased by such factors as individual susceptibility, climatic differences, smoking habits, etc., all of which may affect the response.

#### 6.6 Personal protection

In situations where the measures taken to prevent dust from entering the air remain inadequate, the use of personal protective devices may have an important place in reducing the hazard to the worker. Since an offending agent may be present as particulate matter, gases, fumes, or vapors -- and the exposure take place principally by inhalation -- respiratory protective devices are the most important. Personal protective equipment should not be used in lieu of environmental and engineering controls whenever these are feasible. Such devices are briefly described below; more detailed information

Respirators (air purifying type). Respirators of this type purify air by drawing the contaminated air through a medium that removes most of the contaminant. Filtering facepiece respirators, so-called disposable or single use respirators, have a facepiece that covers the nose and mouth. The respirator is made either entirely of filtering material or by combining filtering material with a plastic or rubber seal. These are discarded after use. They should not be confused with simple nuisance dustmasks, which filter only large particles. Half-mask and quarter-mask respirators usually consist of a rubber or plastic facepiece which covers the nose and mouth and are equipped with replaceable filter cartridges.

Full-facepiece respirators are designed to cover the eyes in addition to the nose and mouth. They are equipped with replaceable canisters. Powered air purifying respirators consist of a battery powered fan which draws air through a filter. The purified air is blown into a half-mask, full-facepiece, or hood. Powered visor respirators have been further developed from the powered air purifying respirator. The fan and the filtered air are blown down behind a protective visor and pass the wearer's face (Else, 1981).

The selection of respiratory protective equipment must always be based on an evaluation of the hazards. The evaluation should take into account the harmful characteristics of the dust in question; the distribution of particle size; the physical and chemical form in which the substances are present, the concentration of the contaminant in the air and its recommended maximum permissible concentration; the frequency and the duration for which the respirator should be used; and the circumstances under which the work is being done.

The use of respirators is always linked with various degrees of discomfort and their use in workers having significantly impaired cardiopulmonary function is currently under investigation. In certain individuals it may be difficult if not impossible to obtain an appropriate fit for air purifying respirators. Workers are understandably reluctant to wear respirators and should therefore be trained and motivated to use them where environmental and engineering controls are inadequate. It is also of the utmost importance that workers are trained in the correct use and maintenance of their respirators (Morse & Miller, 1983). Tasks are difficult to perform for more than 1-2 hours when respirators are worn.

The new so-called airstream helmets have been suggested as a solution because they offer less resistance to breathing and are therefore often acceptable to workers (for instance by farmers working for relatively short periods with moldy hay). However, for a person who already has experienced an acute attack of hypersensitivity pneumonitis, even a IIB filter with its filtering capacity of about 98% of the particles smaller than one micrometer may be inadequate to prevent a new attack (Hendrick et al., 1981). The best protective device would be a ventilated helmet with fresh air supply, a rather expensive solution and not practical in all situations (Terho, 1982).

Breathing apparatuses (supplied air type). Breathing apparatus can be divided into three main types (Else, 1981): 1) fresh-air hose apparatuses which draw air from an adjacent noncontaminated area; 2) compressed airline apparatuses which provides air suitable for respiration through a flexible hose attached to a compressed airline; and 3) self-contained apparatuses which provide air or oxygen from a container carried on a harness attached to the

user's back or chest. Because of their sophistication and complexity, breathing apparatuses are rarely used by workers to provide protection from exposures to dust during normal operations.

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Limitation of the duration of exposure. Limiting the time workers are exposed to harmful dusts can be a means of reducing overall exposure. If respirators are considered necessary, limiting exposure duration in a particular area may also be necessary to control exposure. The physical strain and climatic circumstances may also affect the recommendable duration.

#### 6.7 Health surveillance and training

Preplacement medical examination. The preplacement health examination serves three purposes. One is to ensure that the applicant is physically and mentally fit to undertake the job in question without a health risk to himself or to anyone else. Second, it is important to identify persons who, owing to constitutional or other individual characteristics, may be susceptible to a certain exposure. Third, the examination provides baseline data which makes it possible to detect deviations in health at an early stage (Taylor & Raffle, 1981).

The effectiveness of health surveillance programs depends in part upon the willingness of exposed workers to fully cooperate in such programs. Where periodic surveillance results in a medical finding that a worker is unsuitable for continued employment in jobs with hazardous exposures, the workers should, where possible, be offered alternative, safe employment at comparable pay. In the absence of such alternatives, these workers will likely view surveillance

programs as constituting a potential economic risk rather than as a health protection measure. Under such circumstances, workers will be reluctant to fully participate in surveillance programs, particularly in the reporting of subjective symptoms.

The preplacement examination of workers entering an industry where a known hazards due to dust, fumes, gas, or vapors exists comprises a detailed medical history which should also include the personal and family history of allergy. Emphasis should be placed on present symptoms, whereas childhood symptoms and family history should not be given undue weight. A carefully taken history can never be outdone by sophisticated laboratory or other tests. In general, persons suffering from a chronic chest disease such as chronic bronchitis, emphysema, or bronchial asthma should be carefully evaluated, advised regarding potential health risks, and administratively reviewed before undertaking dusty work or work associated with irritants. Also chronic nasal obstruction, unless it can be corrected by surgery, should be considered reason to administratively review work assignments associated with exposure to dusts or aerosols. Preexistent bronchial hypersensitivity may also renders the applicant unsuitable for work where he would be exposed to dusts or airborne irritants; however, it should be kept in mind that a respiratory viral infection can induce a reversible hyperreactivity of the bronchial tree which may last for several weeks (Little et al., 1978; Simonsson, 1982).

In normal occupational health practice, the determination of ventilatory capacity and the diffusion capacity is sufficient. The ventilatory capacity of the lungs can be recorded using a spirometer. Useful parameters are the forced expiratory volume in one second ( $FEV_1$ ) and the forced vital capacity

(FVC). Since it affects small airways (i.e., airways with a diameter smaller than two millimeters), the forced mid-expiratory flow rate (FMF) may be an indicator of early disease. The more sophisticated maximum expiratory flow volume curves are being increasingly used in well equipped health centers, but for routine occupational health practice, this test offers little advantage over traditional spirometry (Bailey, 1981).

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More important than the sophistication of an apparatus is its proper use. The recording of a normal spirometry conceals a multitude of error sources. The person who performs the test needs to be well trained. In workplaces where the worker can be exposed to irritants or agents that may cause hypersensitivity pneumonitis, it is always advisable to measure the gas transfer capacity. Baseline information may be valuable in order to detect a fibrosing lung disease and to differentiate between such a condition and possible preexistent causes of a decreased diffusion capacity. In order to preclude difficulties in differential diagnosis, smokers should be thoroughly examined at the preplacement stage.

Chest radiography has normally been a means of worker surveillance in dusty occupations associated with the risk of pneumoconioses. In most occupations where the worker may be exposed to vegetable or other natural dusts, chest radiography is of little importance. In operations where an insidious form of hypersensitivity pneumonitis may be suspected, a preplacement chest radiograph may be of some value at a later date. It should be noted that miniature radiographs do not suffice when early fibrotic changes are sought.

Screening for atopy at the preplacement examination, though rarely advisable, may in certain instances have some value if the work is associated with heavy exposure to common, naturally occurring allergens such as pollens, animal epithelium, or house dust mites and if there is reason to suspect that the applicant may be sensitized to the allergens at issue. Routine skin testing should not be performed.

There is tremendous individual variation in susceptibility to sensitizing substances. Persons with a propensity to acquire an allergic disease may do so even after exposure to small concentrations of the offending agent. Permissible levels do not, and for practical reasons cannot, protect the most susceptible individuals. It is therefore of the utmost importance that the characteristics responsible for individual vulnerability be defined and detectable at the preplacement examination. Unfortunately, little is known about individual susceptibility. Atopy as such is a hereditary characteristic undoubtedly associated with an increased risk of sensitization to some agents. However, epidemiological evidence of this increased risk has been found for only a few substances, including biological detergents (Belin et al., 1970; Juniper et al., 1977), platinum salts (Cromwell et al., 1979), locusts (Burge et al., 1979), and grain dust (Parkes, 1982; Davies & Pepys, 1977).

For individuals working with laboratory animals, asthma appears to be a more common outcome among atopics than nonatopics, although the prevalence of all kinds of allergy is as common to one group as it is to the other (Cockroft et al., 1981; Slovak & Hill, 1981; Newman Taylor, 1982). Still, there is no reason to believe that the exclusion of atopic individuals from this industry

would eradicate occupational asthma, let alone other allergies. It would, however, mean that a considerable proportion of workers applying for jobs would be excluded without knowing whether the exposures would ever cause any harm at all.

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The medical criteria for administrative decisions which may result in exclusion of atopics from a particular task involves certain considerations including: 1) how large a proportion of a given population is atopic; and 2) what is the frequency of occupationally related atopy in a given industry? First, the prevalence of atopy (i.e., positive skin tests to common allergens) in various studies may be as high 30-50% (Barbee et al., 1976; d'Souza & Davies, 1977; Woolcock et al., 1978): Second, it appears evident from recent studies on laboratory animals workers that any reduction in health risks achieved by exclusion may be disappointingly low (Cockroft, 1981).

It is as important to realize that the exclusion of atopics cannot prevent asthma or other allergies for the following reasons: 1) even individuals without any demonstrable atopy may become specifically sensitized, thereby producing specific IgE antibodies to a substance, if the exposure is strong enough or if the sensitizing properties of the allergen are strong; both of these conditions are typical in many occupational settings; and 2) occupational asthma is caused by several mechanisms other than the immediate type I reaction responsible for atopy; a direct irritant or toxic effect or a breakdown in control of pharmacologic mediator release may well be the mechanism behind occupational asthma.

In view of both the large proportion of atopics within the general population and the paucity of epidemiologically derived data on the importance of atopy in relation to various specific exposure, it seems wise to restrict the exclusion of atopics to only those situations where present symptoms are thought by responsible administrators to render a worker unsuitable. In cases where atopic workers are known to have an increased risk, they can be advised as to the possible hazards involved and provided, where possible, with other employment opportunities. Atopy is not a risk factor with respect to hypersensitivity pneumonitis (Parkes, 1982).

Training for health and safety. It is extremely important that workers and management be informed about exposures and hazards associated with the new job. Symptoms that may be caused by various exposures ought to be explained and the importance of reporting any symptoms to the occupational health service should be emphasized.

Newcomers should be advised on how exposure can be avoided through effective, well maintained engineering and environmental controls coupled with good work practices, good housekeeping, and the use of appropriate, well maintained personal protective equipment.

Periodic health examinations. The main purposes of periodic health examinations include the evaluation of the effectiveness of preventive measures and the identification of workers susceptible to a particular type of exposure (Schilling, 1981). The fact, that the yield of periodic examinations in terms of significant pathological findings is small, should not discourage occupational health personnel; it should rather be interpreted as an indication of the sufficiency and effectiveness of other preventive measures.

In dusty occupations associated with a risk of pneumoconiosis, periodic examinations are generally performed every second or third year. In workplaces where exposure may lead to sensitization, it is usually advisable to have the first periodic examination two to three months after the preplacement examination, followed by another examination after one year of employment. The rationale for this schedule is that more than half of the workers who will become sensitized to agents such as isocyanates do so within one year.

A detailed history of symptoms remains the most important part of a periodic examination. Spirometry normally is one component of a periodic examination in occupations associated with dusts or irritants. Measurement of the gas transfer capacity depends on respiratory and other symptoms as well as on the type of exposure. In moldy operations, measurement of the gas transfer capacity may be of value even as a routine procedure.

Biological monitoring has been extremely useful in many occupations associated with exposure to toxic agents such as lead, carbon monoxide, and trichloroethylene. In cases of exposure to vegetable and other natural dusts, biological monitoring has not yet been applied routinely. It is conceivable that the presence of antibodies, as demonstrated by skin tests or serological methods in the sera of exposed workers, could offer a means for the biological monitoring of exposed workers (Basich et al., 1980). However, prospective studies on the predictive value of such a practice have not been studied extensively. The extent to which precipitins predict hypersensitivity pneumonitis is still obscure; precipitating antibodies can, however, be used as an indicator of exposure. It is possible that, in the future, immunological methods may serve as a means of biological monitoring.

### 6.8 Cessation of smoking

The importance of ensuring that management, health professionals, and workers understand the critical contribution of cigarette smoking to the general etiology of chronic obstructive lung disorders, can hardly be overemphasized. This is specifically important where obstructive pulmonary disease is caused at least in part by long term repeated exposures to excessive levels of vegetable and other natural dusts. Where feasible and practicable, cigarette smoking should be discouraged and smoking cessation programs made available to assist individuals who wish to stop smoking. Full support of employer's and employee representatives is usually necessary to mount an effective smoking cessation program.

### 6.9 Research priorities

The predictive value of precipitating antibodies in the sera of workers exposed to various microorganisms needs to be assessed.

The development of the insidious type of hypersensitivity pneumonitis should be investigated and its relationship with long-term exposure to low concentrations of spores should be studied.

The basic mechanisms behind occupational asthma should be investigated with respect to various agents. Animal models should be developed.

Atopy increases the risk of sensitization to some agents such as platinum salts and flour, whereas it does not with respect to others, (e.g., isocyanates). More data are needed in order to define the types of exposure

that constitute an increased risk of sensitization for atopics. Longitudinal studies are needed to find out how atopics, with and without symptoms, manage in various occupations associated with exposure to vegetable and other natural dusts. Recommendations as regards atopy should always be based on such data.

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Little is known about the prognosis of occupational asthma and the effect - on its reversibility - of continued exposure to the offending substance.

Prospective studies should be done on the long-term effects of exposure to irritants causing nonspecific irritation in the respiratory tract, manifested as symptoms of bronchitis. The question of whether such exposure eventually leads to chronic bronchitis should be settled.

Research on protective equipment suitable for protection from exposure to sensitizing agents should continue.

Dose-response relationships for various dusts are necessary in order to achieve permissible levels for such materials in the working environment.

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WHO/NIOSH INTERNATIONAL WORKSHOP ON RESPIRATORY DISEASES  
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