

REVIEW

FUNGAL AND ACTINOMYCETE SPORES AS POLLUTANTS OF THE WORKPLACE AND OCCUPATIONAL ALLERGENS*

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Abstract—Spores of fungi and actinomycetes are almost always present in air but their numbers and types differ with time of day, weather, season and location (especially if this is dominated by large nearby spore sources). Without a source of spores in a building, numbers indoors are usually smaller than outdoors but the types found are similar. Heaviest exposure to airborne spores is often found in the workplace. Important sources are agricultural crops, especially during harvesting or during handling and processing after storage, mushrooms, wood for timber or pulping, composts, food processing and, increasingly, biotechnological processes. Many of the spores concerned are 1–5 μm in diameter and they may number up to 10^{10} spores m^{-3} air. Many of the organisms found are well-known allergens and have been implicated in occupational asthma or extrinsic allergic alveolitis. Some may also cause infection, e.g. *Aspergillus fumigatus*, or carry mycotoxins, e.g. *Aspergillus flavus*, while very intense exposure may cause 'organic dust toxic syndrome'. Important factors in the development of occupational asthma and allergic alveolitis are predisposition and the nature, intensity and duration of exposure. Examples of exposure to fungal and actinomycete spores in different occupational environments are described.

INTRODUCTION

MICRO-ORGANISMS, chiefly spores of fungi, are almost always present in the air but their numbers and types change with time of day, weather, season, geographical location and the presence of local spore sources. *Cladosporium* and *Alternaria* species predominate during the day in dry weather throughout much of the world, especially in summer. By contrast, ascospores and basidiospores with active spore release mechanisms predominate at night and after rain. Numbers may exceed 10^6 spores m^{-3} air when the weather is favourable for sporulation and spore liberation but total concentrations of airborne spores are usually of the order of 10^3 – 10^4 m^{-3} air (LACEY, 1981).

Growing crops form immense sources of spores out of doors and large numbers may be liberated during agricultural operations such as harvesting (DARKE *et al.*, 1976). Indoors, numbers of micro-organisms are usually smaller than outdoors unless there is a source of contamination within the building. Such sources include stored products and foods, timber, composts, air conditioning systems and, increasingly, biotechnological processes. Sometimes these can give rise to concentrations of airborne micro-organisms in excess of 10^{10} m^{-3} air. Many of these micro-organisms are 1–5 μm in diameter and well suited for deep penetration into the lung.

For most of the time and for most people, the numbers of micro-organisms

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encountered in the air and inhaled are of little consequence but for some they can be the cause of respiratory disease, its nature and type depending on the immunological constitution of the subject, the nature of exposure and the micro-organisms present (LACEY *et al.*, 1972). This paper reviews the nature of the health effects caused by airborne fungal and actinomycete spores and the environments in which they can present health hazards, while the paper presented by TOPPING *et al.* (1989) at the same conference reviews methods of sampling airborne micro-organisms and antigens.

HEALTH EFFECTS OF INHALED SPORES

Inhalation of organic dusts containing fungal and actinomycete spores can cause a range of respiratory symptoms. Apart from infection, four types of respiratory reaction can be recognized.

Allergic rhinitis and asthma

Allergic rhinitis and asthma depend largely on a constitutional predisposition of the subject, known as atopy, which allows sensitization by normal, everyday exposure to airborne allergens. The incidence of occupational asthma is variable but it is estimated that this accounts for 5–15% of all asthma (BUTCHER and SALVAGGIO, 1986). Farmers are exposed to many of the same allergens as the general population and the incidence of atopy is probably similar in the two groups so that it is probably not surprising that the incidence of allergy and asthma is similar in the two groups (HEINONEN *et al.*, 1987). However, many fungal allergens originate from agricultural crops, especially close to harvest (e.g. *Cladosporium*, *Alternaria*, *Didymella* spp.), and from stored feeds and seeds (e.g. *Aspergillus fumigatus* and other *Aspergillus* and *Penicillium* spp.; LACEY, 1980a, 1981; HARRIES *et al.*, 1985).

Chronic bronchitis

The role of airborne spores in causing bronchitis is uncertain and is perhaps non-specific or associated with endotoxins from Gram-negative bacteria. Incidence is greater among atopic subjects, suggesting an allergic component, and both atopy and smoking have additive effects on incidence (DONHAM *et al.*, 1984; TERHO *et al.*, 1987). However, among farmers, it occurs more frequently than in the general population. It is particularly associated with swine and poultry confinement buildings and with grain handling. Its incidence in other occupations exposed to organic dusts is uncertain.

Extrinsic allergic alveolitis (hypersensitivity pneumonitis)

Extrinsic allergic alveolitis is a T-lymphocyte dependent granulomatous inflammatory reaction, predominantly of the peripheral gas exchange tissue of the lung that does not depend to any great extent on constitutional predisposition (NEWMAN TAYLOR, 1987). It is caused by a variety of dusts containing both fungal and actinomycete spores, is characteristically an occupational disease and the names given to the different forms usually reflect the environment in which they occur or the source of the antigen. Farmer's lung is the classic example of an allergic alveolitis. Apart from micro-organisms, allergic alveolitis may be caused by avian and animal serum proteins. A characteristic of the aetiology of the diseases caused by fungi and actinomycetes is

repeated exposure to large concentrations of spores mostly 1–5 μm in diameter. Concentrations typically exceed 10^6 spores m^{-3} air (LACEY *et al.*, 1972) and a minimum concentration of 10^8 has been suggested for the causation of acute symptoms (RYLANDER, 1986) although this remains unproven. Insidious development of chronic allergic alveolitis, without acute symptoms, may be the consequence of prolonged exposure to relatively low spore concentrations.

Acute symptoms of allergic alveolitis develop several hours after exposure to the offending dust and include chills, fever, a dry cough, malaise and, with repeated exposure, increasing breathlessness and weight loss. Eventually, permanent lung damage may occur. Diagnosis is based on a history of exposure to the relevant antigen, clinical, radiographic and functional changes typical of the disease and the presence of precipitating IgG antibodies (precipitins) to the causal antigen, with the possible presence of basal crepitant rales, impairment of pulmonary diffusing capacity, decreased arterial oxygen tension, a restrictive ventilation defect, increased lymphocytes and granulomatous infiltrations and with reproduction of the disease in inhalation challenge with a relevant antigen (DO PICO, 1986; TEE and NEWMAN TAYLOR, 1987). Precipitins are indicative of exposure to antigen and their relevance to the disease has to be proved.

Organic dust toxic syndrome

Organic dust toxic syndrome, also referred to as silo unloader's disease and pulmonary mycotoxicosis, can share some of the features of allergic alveolitis. It also requires intense exposure to airborne dust and results in influenza-like symptoms with leukocytosis and fever but it appears to require no prior sensitization, antibodies do not develop, respiratory symptoms may or may not occur and there are usually no radiographic changes. Also many workers exposed at one time may be affected. Fungi, bacteria, mycotoxins and endotoxins have all been suggested as possible causes (EMANUEL *et al.*, 1975; BURG *et al.*, 1981, 1982; BURG and SHOTWELL, 1984; PRATT and MAY, 1984; RYLANDER, 1986; DO PICO, 1986; PRATT *et al.*, 1986; LECOURS *et al.*, 1986). Endotoxins from Gram-negative bacteria are known to produce febrile reactions on inhalation. However, the aerobiology of environments in which this syndrome has occurred has never been defined nor the roles of the different micro-organisms established.

EXPOSURE TO FUNGAL AND ACTINOMYCETE SPORES IN OCCUPATIONAL ENVIRONMENTS

Fungi implicated in occupational asthma

Occupational asthma has been reported during work in both outdoor and indoor environments (Table 1). Out-of-doors the boundary between what might be considered normal, everyday exposure and occupational exposure is indistinct. Exposure to fungal spores occurs continuously and many of the species present in the normal air spora are known to cause allergic rhinitis and asthma (HYDE, 1972; BURGE, 1985). The best known of these are *Cladosporium* and *Alternaria* which grow abundantly on agricultural crops and form a large proportion of the natural air spora but whose concentrations in the air are enhanced by agricultural operations such as hay making and harvest.

TABLE 1. FUNGI IMPLICATED IN OCCUPATIONAL ASTHMA

Source of allergen	Fungus implicated	Reference
Outdoor environments		
Cereal grains and straw	<i>Puccinia</i> spp. <i>Ustilago</i> spp. <i>Tilletia caries</i> <i>Verticillium lecanii</i> <i>Aphanocladium album</i> <i>Paecilomyces farinosus</i>	CADHAM, 1924 HARRIS, 1939 JIMENEZ-DIAZ <i>et al.</i> , 1947 DARKE <i>et al.</i> , 1976
Reeds	<i>Apiospora montagnei</i> (<i>Arthrimum arundinis</i>)	DUCHÉ, 1944
Indoor environments		
Mushroom culture	<i>Aspergillus fumigatus</i> <i>Lentinus edulis</i> <i>Pleurotus ostreatus</i>	SAKULA, 1967 KONDO, 1969 ZADRAZIL, 1974; SCHULZ <i>et al.</i> , 1974 OLIVIER <i>et al.</i> , 1975
Enzyme production (surface culture)	<i>Oidiodendron</i> sp. <i>Aspergillus flavus</i> <i>Aspergillus awamori</i>	IZRAILET and FEOKTISTOVA, 1970
Food protein culture	<i>Candida tropicalis</i>	CORNILLON <i>et al.</i> , 1975
Flour	<i>Alternaria</i> spp. <i>Aspergillus</i> spp.	KLAUSTERMEYER <i>et al.</i> , 1977
Soup manufacture	<i>Agaricus hisporus</i> <i>Boletus edulis</i>	SYMINGTON <i>et al.</i> , 1981
Cheese dairy	<i>Penicillium camembertii</i>	GARI <i>et al.</i> , 1983
Tobacco	<i>Scopulariopsis brevicaulis</i>	LANDER <i>et al.</i> , 1985
Chiropodist's practice	<i>Trichophyton rubrum</i>	PEPYS, 1986

Occupational exposure indoors is easier to define since it relates to spores from indoor sources, with a species composition that differs markedly from normal everyday exposure. Without an indoor source of spores, the types in the air will be similar to those outdoors but numbers will be smaller by perhaps two-thirds (BURGE *et al.*, 1987). Such small numbers are overwhelmed by spores, typically of storage fungi and actinomycetes, from indoor sources. Occupational asthma in which fungal spores have been implicated has been reported in many working environments (Table 1) but in most of these levels of exposure have not been determined.

Fungi implicated in allergic alveolitis

When allergic alveolitis occurs, it is almost invariably in indoor environments and it is characteristically occupational (Table 2). The fungi implicated are chiefly dry spored species producing abundant spores smaller than 5 μm . They include several *Aspergillus* and *Penicillium* species. Exceptionally, allergic alveolitis may be caused by slimy spored species, such as *Graphium* sp., *Aureobasidium pullulans*, *Phoma violacea* and *Acremonium* spp., which become airborne in aerosols created by showers or humidifiers or through the action of sawmills, or by basidiospores of mushrooms, liberated in large numbers by some species. The role of fungi in allergic alveolitis of woodworkers is somewhat controversial. Late asthmatic responses have been found in patients exposed to wood dust alone (PICKERING *et al.*, 1972) but BELIN (1980, 1987) and MAIER *et al.* (1981) consider that such symptoms can be caused by moulds in a similar manner to sequoiosis (COHEN *et al.*, 1967).

TABLE 2. FUNGI IMPLICATED IN ALLERGIC ALVEOLITIS

Source of antigen	Fungus implicated	Reference
Mouldy, heated grain	Unspecified	RAMAZZINI, 1713
Malting barley	<i>Aspergillus fumigatus</i>	DUNNER <i>et al.</i> , 1946
	<i>Aspergillus clavatus</i>	VALLERY-RADOT and GIROUD, 1928
Citric acid fermentation	<i>Penicillium</i> spp.	RIDDLE <i>et al.</i> , 1968
	<i>Aspergillus fumigatus</i>	HOŘEŠÍ <i>et al.</i> , 1960
	<i>Aspergillus niger</i>	
Maple bark	<i>Cryptosporium corticale</i>	TOPPING <i>et al.</i> , 1985
Redwood sawdust	<i>Graphium</i> spp.	EMANUEL <i>et al.</i> , 1962
	<i>Aureobasidium pullulans</i>	COHEN <i>et al.</i> , 1967
Cheese	<i>Penicillium casei</i>	DE WECK <i>et al.</i> , 1969
Straw	<i>Aspergillus versicolor</i>	MOLINA <i>et al.</i> , 1971
Shower curtain	<i>Phoma violacea</i>	RHODY <i>et al.</i> , 1971
Maize grain	<i>Aspergillus flavus</i>	GREEN <i>et al.</i> , 1972
Cork	<i>Penicillium glabrum</i> (<i>P. frequentans</i>)	PATTERSON <i>et al.</i> , 1974
Mushroom culture	<i>Pleurotus ostreatus</i>	AVILA and LACEY, 1974
	<i>Pholiota nameko</i>	SCHULZ <i>et al.</i> , 1974
Oat grain	<i>Aspergillus fumigatus</i>	TOCHIGI <i>et al.</i> , 1982
Hay	<i>Aspergillus umbrosus</i>	YOCUM <i>et al.</i> , 1976
Humidifiers	<i>Penicillium</i> spp.	TERHO and LACEY, 1979
	<i>Acremonium</i> spp.	SOLLEY and HYATT, 1980
	<i>Aspergillus fumigatus</i>	PATTERSON <i>et al.</i> , 1981
Timber	<i>Rhizopus microsporus</i> var. <i>rhizopodiformis</i>	VAN ASSENDELFT, 1985
	<i>Penicillium</i> spp.	BELIN, 1980
	<i>Aspergillus fumigatus</i>	VAN ASSENDELFT <i>et al.</i> , 1985
	<i>Trichoderma viride</i> (?)	BELIN, 1987
		SCHMITZ-SCHUMANN <i>et al.</i> , 1986
Mouldy walls	<i>Penicillium casei</i>	TÖRÖK <i>et al.</i> , 1981
	<i>Aureobasidium pullans</i>	
	<i>Cladosporium</i> sp.	JACOBS <i>et al.</i> , 1986
Decaying timber	<i>Serpula pinastri</i>	GARFIELD <i>et al.</i> , 1984
Compost	<i>Aspergillus fumigatus</i>	VINCKEN and ROELS, 1984
Tobacco	<i>Aspergillus fumigatus</i>	HUUSKONEN <i>et al.</i> , 1984
Sausage	<i>Penicillium jensenii</i>	MORIN <i>et al.</i> , 1984
		GÉRAULT <i>et al.</i> , 1984
Rabbit farm	<i>Aspergillus clavatus</i>	DE CLOSETS <i>et al.</i> , 1985
Apple store	<i>Penicillium</i> spp.	KROIDL <i>et al.</i> , 1984
	<i>Alternaria alternata</i>	

Actinomycetes implicated in allergic alveolitis

With few exceptions, the actinomycetes implicated in allergic alveolitis (Table 3) are thermophilic species that grow in stored products that have heated to temperatures up to 65–70°C during storage following inadequate drying or during composting (GREGORY *et al.*, 1963; FESTENSTEIN *et al.*, 1965; LACEY, 1974, 1980b). Under these conditions, populations up to 10^{10} spores g^{-1} substrate can develop. These spores are easily dispersed into the air by disturbance of the substrate. Farmer's lung is the classic form of allergic alveolitis and the thermophilic actinomycete, *Faenia rectivirgula* (*Micropolyspora faeni*) is considered the principal source of antigens in the United Kingdom. However, in sera from farmer's lung patients from Finland, Switzerland, Canada and the U.S.A., antibody titres were greatest in the U.S.A. to *F. rectivirgula* and in the other countries to *Thermoactinomyces vulgaris* (KURUP *et al.*, 1987). Titres to

T. vulgaris and *T. thalophilus* in Finnish sera were similar, contrasting with earlier studies in which antibodies to *T. vulgaris* predominated (TERHO and LACEY, 1979) but in Swiss and Canadian sera, titres to *T. vulgaris* were the greater.

The only mesophilic actinomycetes to be implicated in allergic alveolitis were *Streptomyces olivaceus* and *S. albus*. *S. olivaceus* was isolated from the thatch of dwellings in New Guinea and caused allergic alveolitis in guineapigs although its role in human disease could not be confirmed. *S. albus* was found in 'plant dirt' used industrially to prepare bacterial inoculants for legume crops in the U.S.A. and caused symptoms of allergic alveolitis in an exposed worker when he was challenged with extracts of the actinomycete (KAGEN *et al.*, 1981); it is also common in mouldy hay and grain (FESTENSTEIN *et al.*, 1965) and in the air of farm buildings but has not been shown to cause allergic alveolitis in these environments.

CIRCUMSTANCES OF EXPOSURE TO FUNGAL AND ACTINOMYCETE SPORES IN SELECTED ENVIRONMENTS

The exposure of workers to fungal and actinomycete spores in occupational environments is seldom constant but changes both quantitatively and qualitatively. The nature and extent of the air spora in such environments is determined by the degree of colonization of the substrate, how much it is disturbed and by the effectiveness of ventilation. How these factors affect occupational exposure of workers will be illustrated by reference to selected environments.

The farm environment

Growing and stored crops form vast sources of fungal and actinomycete spores. However, the spore types and the numbers that they contribute to the working environment change with the source of spores and, with stored products, with the conditions of storage, degree of disturbance and ventilation. The distinction between everyday and occupational exposure is nowhere more difficult to draw than on the farm. The fungi that colonize growing crops are those that predominate in the air, both by day and by night, and are those that are dispersed during haymaking, harvesting and other agricultural operations. Harvesting can lead to concentrations exceeding 10^8 spores m^{-3} air near to the cutter bar and straw discharge and about 10% of this near the driver (DARKE *et al.*, 1976). Up to 75% of these may be *Cladosporium*, 25% *Alternaria* and 10% *Verticillium* type spores. Rust or smut diseases within the crop will increase the contribution from *Puccinia* and *Ustilago* to 3–4% or more. Exposure of the workers can be decreased by using helmets or cabs with filtered air supplies. These can remove up to 98% of spores from the breathing zone (LACEY and MCLEAN, 1977).

With storage, the nature of the microflora in hay and grain usually changes, the field microflora becoming replaced by species typical of storage. The predominant species are determined by storage conditions, especially temperature and water content. Species present before harvest survive only in hay or grain stored dry, with water contents of 12–13%. As water content increases, other species are able to grow and increasing metabolic activity leads to spontaneous heating (Table 4; LACEY, 1980b; LACEY *et al.*, 1980). With water contents greater than 35%, temperatures of 65°C may be attained allowing the growth of thermophilic and thermotolerant fungi and actinomycetes, including species that can cause infection (*Aspergillus fumigatus*,

TABLE 3. ACTINOMYCETES IMPLICATED IN ALLERGIC ALVEOLITIS

Source of antigen	Actinomycetes implicated	Reference
Hay (farmer's lung)	<i>Faenia rectivirgula</i>	PEPYS <i>et al.</i> , 1963
	<i>Thermoactinomyces vulgaris</i>	TERHO and LACEY, 1979
	<i>Thermoactinomyces thalpophilus</i> , (as <i>T. vulgaris</i>)	PEPYS <i>et al.</i> , 1963
	<i>Saccharomonospora viridis</i>	BARROWCLIFF and ARBLASTER, 1968
Bagasse	<i>Thermoactinomyces vulgaris</i>	GREENE <i>et al.</i> , 1981
Mushroom compost	<i>Thermoactinomyces sacchari</i>	HARGREAVE <i>et al.</i> , 1968
	<i>Faenia rectivirgula</i>	LACEY, 1971a
	<i>Thermoactinomyces vulgaris</i>	SAKULA, 1967
Humidifiers	<i>Thermoactinomyces dichotomicus</i>	MOLINA <i>et al.</i> , 1982
	<i>Saccharomonospora viridis</i>	KURUP, 1984
	<i>Thermoactinomyces thalpophilus</i>	KURUP <i>et al.</i> , 1976
	<i>Thermoactinomyces vulgaris</i>	
	<i>Saccharomonospora viridis</i>	
Thatch Plant litter	<i>Thermoactinomyces intermedius</i>	KURUP <i>et al.</i> , 1980
	<i>Streptomyces olivaceus</i> (?)	BLACKBURN and GREEN, 1974
	<i>Streptomyces albus</i>	KAGEN <i>et al.</i> , 1981

Absidia corymbifera, *Rhizomucor pusillus*), asthma (*A. fumigatus*) and allergic alveolitis (*Faenia rectivirgula*, *Thermoactinomyces* spp.; GREGORY *et al.*, 1963; PEPYS *et al.*, 1963; FESTENSTEIN *et al.*, 1965). Development of antibodies to *F. rectivirgula* may be positively correlated with size of farm, time spent in the barn and a family history of farmer's lung, but not, surprisingly, with presence of mouldy hay or method of storage (CORMIER *et al.*, 1985).

TABLE 4. THE EFFECT OF STORAGE CONDITIONS ON THE PREDOMINANT MICRO-ORGANISMS IN HAY AND GRAIN (AFTER LACEY *et al.*, 1980)

Approximate water activity (aw)	Approximate water content (%)	Likely maximum temperature (°C)	Predominant species
0.7-0.8	14.0-16.6	ambient	<i>Aspergillus restrictus</i>
0.8-0.9	16.6-20.3	35	<i>Eurotium</i> spp. (<i>Aspergillus glaucus</i> group)
0.9-0.95	20.3-24.8	40	<i>Aspergillus versicolor</i> group <i>Scopulariopsis brevicaulis</i> <i>Streptomyces griseus</i>
0.95	24.8	45	<i>Aspergillus candidus</i> , <i>Penicillium</i> spp.
0.98	30.0	50-55	<i>Aspergillus nidulans</i> <i>Absidia corymbifera</i> <i>Streptomyces albus</i>
1.0	40.0	65	<i>Aspergillus fumigatus</i> <i>Rhizomucor pusillus</i> <i>Humicola lanuginosa</i> <i>Saccharomonospora viridis</i> <i>Faenia rectivirgula</i> <i>Thermoactinomyces</i> spp.

Traditional methods of hay making in Finland, with long periods of drying on racks, decrease heating and the incidence of *F. rectivirgula* although *Thermoactinomyces* spp. and *Eurotium* spp. (members of the *Aspergillus glaucus* group) remain abundant with antibodies to both in farmer's lung patients (TERHO and LACEY, 1979). However, in later studies, *T. vulgaris*, *F. rectivirgula* and *Aspergillus umbrosus* were all more abundant on farms with farmer's lung patients than on those without (KOTIMAA *et al.*, 1984, 1987). In Canadian grain elevators, *Aspergillus* and *Penicillium* spp. predominate in settled dust but actinomycetes may also be found (WILLIAMS *et al.*, 1964; LACEY, 1980a) and may contribute to respiratory disorders (DENNIS, 1973). There are often close inter-relationships between mite and fungal development in hay and grain which may result in mite allergy in exposed workers (CUTHBERT *et al.*, 1979; REVSBECK and ANDERSEN, 1987; LESKINEN and KLEN, 1987).

In silos used to store moist barley and maize silage, the microflora may be further modified by changes in the intergranular gas composition. Carbon dioxide concentrations increase sufficiently, as a result of grain and microbial respiration, to inhibit fungal growth. In unsealed silos, a mouldy layer usually develops at the surface, where gaseous exchange can still occur, depending on water content and the nature of any covering. Removal of this can generate vast quantities of actinomycete and fungal spores creating the circumstances in which organic dust toxic syndrome occurs. Once this layer is removed, subsequent heating and moulding is controlled by the rate at which grain is removed from the exposed upper surface of top-unloaded silos. Removal of at least 8 cm daily prevents heating and moulding but slower removal results in colonization first by yeasts then in sequence, *Penicillium roquefortii*, *P. rugulosum* and, with heating, *Absidia corymbifera*, *Rhizomucor pusillus* and finally *A. fumigatus* and *F. rectivirgula* (LACEY, 1971b).

All species of storage fungi and actinomycetes produce abundant spores that easily become airborne when the substrate is disturbed to give up to 10^{10} spores m^{-3} air with numbers and types changing as the microflora of the substrate changes. With heated hays and grains, up to 98% of the airborne spores may come from actinomycetes (BARUAH, 1961; LACEY and LACEY, 1964; LACEY, 1971b, 1988b; ZEITLER, 1986). Such large concentrations may occur not only when hay bales are moved or opened for feeding to cattle but also when moving grain, unloading silos and in docks when loading and unloading ships (LACEY, 1980a, 1988b). In animal houses, concentrations of airborne fungi and actinomycetes are greatest when mouldy hay and grain are being fed. However, mouldy feeds are not the only sources of airborne organic material in animal house dust. The animals may themselves yield airborne skin scales, fur or feathers which may all carry bacteria that contribute to the endotoxin load in the air while aerosols may be formed of urine and faecal material that can be allergenic (THEDELL *et al.*, 1980; HARRIES and CROMWELL, 1982; CLARK *et al.*, 1983; BROUWER *et al.*, 1986; TRAVERS *et al.*, 1988).

Mushroom farms

Preparation of compost on which to grow the common mushroom, *Agaricus bisporus*, involves the spontaneous heating of a mixture of horse manure, straw and other components. After 7–10 days, with occasional turning and heating to 75–80°C, the compost is placed loose or in boxes in steam-heated tunnels in which it is first rapidly heated to 60°C and then maintained above 50°C for several days. During this

last stage, abundant actinomycete growth occurs, chiefly of *Thermomonospora chromogena*, *T. fusca* and *T. curvata* (LACEY, 1973a, 1988a). When mushroom spawn is mixed with the compost and when it moves along conveyors, especially when it drops from one level to another, spores are dispersed into the air in large numbers. Spawning sheds of two farms yielded up to 4×10^8 spores of actinomycetes and bacteria m^{-3} air but only about 10^5 fungal spores m^{-3} , mostly *Scytalidium* (*Torula*) *thermophilum*. Counts of viable actinomycetes were smaller, numbering up to 2×10^6 *Thermomonospora* spp. colony forming units (cfu) m^{-3} air, 1.8×10^6 *T. chromogena* and 2.9×10^5 white *Thermomonospora* spp. Close to the source, workers were exposed to 6.3×10^6 *T. chromogena* spores m^{-3} air. Previously, *F. rectivirgula* and *Thermoactinomyces* spp. have been implicated in mushroom worker's lung (SAKULA, 1967) but these formed only up to 1.5×10^5 cfu m^{-3} air, mostly on the upper stages of the Andersen sampler, contrasting with the *Thermomonospora* spp. found mainly on the lower stages.

In the growing houses, *Agaricus* spores were few when picked as 'buttons' but if the veils ruptured and the caps allowed to open, up to 10^6 spores m^{-3} could be found. Moulds growing on the compost and on the moist timber of the boxes were also present in the air and no doubt many were disturbed during picking, perhaps contributing to asthma in atopic pickers. These included *Cephalotrichum* (*Doratomyces*) *stemmitis* (up to 2.1×10^5 spores m^{-3} air), *A. fumigatus* (up to 9×10^4 cfu m^{-3} air) and *Penicillium* spp. (up to 4×10^4 cfu m^{-3} air). The oyster mushroom, *Pleurotus ostreatus*, grown widely in Europe and sometimes as an experimental crop in England produces spores much more prolifically than *A. bisporus*. These may even be seen rising like a fine mist from the gills in suitable conditions to give concentrations up to 4×10^7 spores m^{-3} air, sufficient to cause allergic alveolitis (SCHULZ *et al.*, 1974; LACEY, 1988a). Oriental mushrooms, like *Lentinus edodes* (Shiitake), may also produce many spores and cause asthma and allergic alveolitis (KONDO, 1969).

Municipal waste composting

Composting may be used to decrease the bulk and to stabilize putrescible municipal waste and sewage. Spontaneous heating to 55–60°C is an important part of the process and the microbiological changes that occur are similar to those in mushroom composts, with some 49% of bacterial colonies formed by *Thermomonospora* and *Thermoactinomyces* spp. in equal numbers. Total bacteria in the breathing zone of workers dismantling a static pile of compost numbered 1.9×10^7 cfu m^{-3} air. Fungi, 93% of which were *A. fumigatus*, numbered 8.2×10^6 cfu m^{-3} air (CROOK *et al.*, 1988a). In France, concentrations of mesophilic fungi up to 7.8×10^4 cfu m^{-3} air and of thermophilic fungi up to 6.1×10^4 cfu m^{-3} air were found in four refuse composting plants. *Penicillium* spp. were common in the raw garbage while *A. fumigatus* increased during composting. Actinomycetes were also common but not identified (BOUTIN *et al.*, 1987). Large numbers of *A. fumigatus* were also dispersed, at a rate of 4.6×10^6 cfu s^{-1} , from composted sewage sludge in the U.S.A. (MILLNER *et al.*, 1980). Thermophilic actinomycetes were also present (GOODFELLOW *et al.*, 1987; LACEY, unpublished).

Food processing

Allergy to spores of *Agaricus bisporus* in a soup processing factory was reported by SYMINGTON *et al.* (1981) but usually exposure to fungal spores during food processing is related to stored products. For instance, coffee beans, prior to roasting, usually carry

fungus spores which can be dispersed into the air. Most (up to 2.4×10^4 cfu m⁻³ air) were found in containers being unloaded at a warehouse. They included *Eurotium* spp., *A. fumigatus*, *A. flavus*, *A. niger* and *Wallemia sebi*. Actinomycetes were few, numbering only 800 cfu m⁻³ air at most. Within the warehouse, exhaust ventilation was effective in decreasing airborne spores in the general environment but workers emptying sacks were still heavily exposed. However, the chief allergen appeared to be green coffee bean dust or, occasionally, castor bean dust contaminating the sacks (CROOK *et al.*, 1988c).

Fungi are frequent in the air of bakeries, especially *Aspergillus*, *Penicillium* and *Mucor* spp. (WALLENSTEIN *et al.*, 1980; CROOK *et al.*, 1988d). Flour and dried fruit are important sources. In a British bakery, up to 1.2×10^3 cfu m⁻³ air, mostly *Penicillium* spp., were found where flour was weighed and up to 3.7×10^3 cfu m⁻³ air, mostly *Wallemia sebi* and yeasts, where dry fruit was handled. Actinomycetes were again few (CROOK *et al.*, 1988d). *Aspergillus* and *Alternaria* spp. and fungal amylase have been suggested as causes of baker's asthma (KLAUSTERMEYER *et al.*, 1977; BAUR *et al.*, 1986) but the aetiology of this condition remains obscure. *Penicillium* spp. are also important in the maturation of some cheeses and sausages and may grow abundantly on the surfaces. When these are cleaned prior to sale the spores are easily dispersed to cause allergic alveolitis in exposed workers (DE WECK *et al.*, 1969; GÉRAULT *et al.*, 1984; MORIN *et al.*, 1984).

Industrial environments

Feed mills are contaminated with the same range of fungi as are found in grain stores on farms, with *Aspergillus* spp. often predominant (STALLYBRASS, 1961). However, when grain is germinated for malting, the conditions of the malt floor favour *Aspergillus clavatus*, especially when germination is poor. Turning the sprouting grain releases the abundant spores into the air, obscuring vision across the floor (RIDDLE *et al.*, 1968).

Sugar cane bagasse, the squashed, chopped fibre left after sugar is extracted from sugar cane, leaves the factory containing 50% water and up to 5% sucrose. It thus forms a good substrate for microbial growth and, when stored in bales, rapidly heats to temperatures above 50°C which it can maintain for a period of 2–3 months (LACEY, 1974). A characteristically thermophilic microflora develops but many of the species differ from those in hay. *A. fumigatus* may be abundant together with thermophilic actinomycetes. *Thermoactinomyces vulgaris* occurs widely in samples but *T. sacchari* occurs much more frequently in large numbers and seems the more likely cause of bagassosis, a form of allergic alveolitis that occurs when mouldy bagasse is handled, as when it is used for particle board manufacture. The species have both common and distinctive antigens (LACEY, 1971a).

Fungal exposure also occurs in sawmills where some of the earliest forms of allergic alveolitis were described. *Cryptostroma corticale* is a pathogen of maple trees in North America. Infection may occur while the tree is standing but the fungus continues to grow under the bark after felling and to produce copious spores that are released when the bark is stripped in the mill. Up to 1.3×10^7 cfu m⁻³ air may be produced causing maple bark pneumonitis in workers (WENZEL and EMANUEL, 1967). *Aureobasidium pullulans* and *Graphium* spp. have similarly been implicated in sequoiosis, associated with redwood in the U.S.A. (COHEN *et al.*, 1967). In Scandinavia, wood is cut into chips for use as fuel and then stored in bulk. Moulding of the chips can occur with the

predominant species including *A. fumigatus*, *A. niger*, *Mucor* spp., *Paecilomyces variotii*, *Penicillium* spp., *Talaromyces* spp., *Trichoderma* spp., *Aureobasidium pullulans*, *Phanerochaete chrysosporium* and *Thermoactinomyces vulgaris* (TERHO *et al.*, 1980; THÖRNQVIST and LUNDSTRÖM, 1982; VAN ASSENDELFT *et al.*, 1985). *A. fumigatus* has also been reported from sawmills, with some isolates producing tremorgenic mycotoxins (LAND *et al.*, 1987) while *Rhizopus microsporus* var. *rhizopodiformis*, from both wood chips and timber, has been implicated in allergic alveolitis (BELIN, 1980). About 50% of Swedish woodtrimmers had precipitins, mostly to *Rhizopus*, and 10–20% were suffering from allergic alveolitis (BELIN, 1985).

The processing of cork may involve submerging the bales for several hours in vats of boiling water and then stacking them for several days in small humid warehouses during which time they become covered with mould growth. The predominant species are *Penicillium glabrum* (*P. frequentans*), *P. granulatum*, *Aphanocladium album*, *Monilia sitophila* and *Mucor plumbeus*. However only *P. glabrum* was abundant throughout the factory and formed precipitins in the sera of cork workers with suberosis. Background concentrations reached 2.6×10^7 spores m^{-3} air in the small warehouses and ranged between 10^6 and 10^7 m^{-3} within the factory where the cork was processed. About half of these were spores of *Penicillium* spp. Workers were exposed to up to 9×10^7 spores m^{-3} air with heaviest exposure when moving the mouldy cork from the warehouse. Fewer spores were associated with cork that had been conditioned by steaming immediately before processing (LACEY, 1973b; AVILA and LACEY, 1974).

Byssinosis is a classic example of an occupational lung disease but its aetiology is still obscure. Bacterial endotoxins have received strong support recently (RYLANDER and SNELLA, 1976; SALKINOJA-SALONEN *et al.*, 1982) but fungi and actinomycetes are also common in the air of cotton mills, numbering up to 4.0×10^5 and 1.2×10^7 m^{-3} air, respectively, in a new mill in northeast England and 1.2×10^6 and 9.8×10^6 m^{-3} , respectively, in an old Lancashire mill. The predominant fungi were *Cladosporium*, *Penicillium* and *Eurotium* spp. and *Aspergillus niger*, all most common in the air during the early stages of processing. Actinomycetes were usually few, mostly *Streptomyces* spp. and *Nocardopsis dassonvillei* but in the Lancashire mill, *F. rectivirgula* and *Thermoactinomyces* spp. were abundant in the air (LACEY and LACEY, 1987).

Biotechnological processes are being increasingly used to produce nutritional proteins, enzymes and other useful metabolites and to degrade wastes and recalcitrant molecules. Aerosols may be produced during the handling of culture mats, through the breaking of liquid films and the leaking of fermenters. Thus, TOPPING *et al.* (1985) could find airborne allergen of *Aspergillus niger* and sensitivity to the spores that were dispersed from surface citric acid fermentations. However, HOŘEJŠÍ *et al.* (1960) found that contaminating *Aspergillus* and *Penicillium* spp. were important causes of allergic alveolitis from similar fermentations in Hungary. Most complaints occurred when *Penicillium* was abundant. Exposure could also occur to *Fusarium* and yeasts used to produce protein and to *Aspergillus* spp. used to produce enzymes but there is currently no evidence of disease caused by the spores of these fungi. With microbial insecticides, exposure to the fungus may occur not only during production but also during application, as with *Verticillium lecanii* by spraying in glasshouses (EATON *et al.*, 1986).

Exposure to fungal spores in industrial environments does not necessarily come from materials but may also originate from air conditioning systems, especially if these are humidified. Water reservoirs and moist baffle plates provide environments for the

growth of fungi, bacteria including actinomycetes, protozoa, nematodes and even aquatic mites. *A. fumigatus* was found colonizing the air conditioning system of a factory producing synthetic fibres (WOLF, 1969), but usually there is a mixture of fungi present (SOLOMON, 1974). These have included *Aureobasidium pullulans*, *Paecilomyces lilacinus*, *Phialophora hoffmannii*, unidentified *Phialophora*, *Phoma*, *Penicillium*, *Fusarium* and *Acremonium* spp. (PICKERING *et al.*, 1976; STORMS, 1978; AUSTWICK, 1982; GRAVESEN and JEPSEN, 1981; BERNSTEIN *et al.*, 1983; SAMSON, 1985). Thermophilic actinomycetes have also been found, particularly in the U.S.A., but not quantified (BANASZAK *et al.*, 1970; LACEY, 1988b). However, the role of fungi and actinomycetes in humidifier fever is uncertain. Many of the components of the microflora have been implicated at different times (LIEBERT *et al.*, 1984; BANASZAK *et al.*, 1970; EDWARDS *et al.*, 1976; RYLANDER *et al.*, 1978; RYLANDER and HAGLIND, 1984) but other studies have failed to confirm earlier conclusions (LONGBOTTOM, 1986; MCSHARRY *et al.*, 1987; FINNEGAN *et al.*, 1987) and there is still little agreement as to the likely cause (EDWARDS, 1986; AUSTWICK *et al.*, 1986).

EXPOSURE TO MICROBIAL PRODUCTS

Exposure to bacterial proteolytic enzymes is well known as a cause of occupational asthma (ZACHARIAE *et al.*, 1982) while antibodies to actinomycete enzymes have been recognized in farmer's lung patients (NICOLET *et al.*, 1977; ROBERTS *et al.*, 1983). It is therefore not surprising that fungal enzymes and other products have also been shown to produce similar disorders during their production and during use in bakeries (Table 5). Although no respiratory responses to actinomycete antibiotics have so far been reported during their production, late asthmatic responses to semi-synthetic penicillins and cephalosporin have been found in antibiotic factories (DAVIES *et al.*, 1974; BUTCHER and SALVAGGIO, 1986).

TABLE 5. FUNGAL METABOLITES IMPLICATED IN OCCUPATIONAL ASTHMA

Metabolite	Source fungus	Reference
Penicillin	<i>Penicillium chrysogenum</i>	DAVIES <i>et al.</i> , 1974
'Flaviastase' (protease)	<i>Aspergillus niger</i>	PAUWELS <i>et al.</i> , 1978
'Brinase' (protease)	<i>Aspergillus oryzae</i>	FORSBECK and EKENVALL, 1978
Cellulase	<i>Aspergillus niger</i>	LOSADA <i>et al.</i> , 1986
Amylase	<i>Aspergillus</i> sp.	BAUR <i>et al.</i> , 1986
Cephalosporin	<i>Acremonium strictum</i>	BUTCHER and SALVAGGIO, 1986

Some mycotoxin-producing fungi also carry the mycotoxin in their spores with consequent hazards to health on inhalation. For instance, dust from groundnuts contained 250–400 ng aflatoxin from *Aspergillus flavus* and *A. parasiticus* g⁻¹, with more than 8% of particles smaller than 5 µm. It was estimated that baggers could inhale 0.04–2.5 µg aflatoxins in a 45 h week, perhaps resulting in lung, liver and colon cancer although interpretation is complicated by the consumption of groundnuts by workers during their work (DVOŘÁČKOVÁ, 1976; DEGER, 1976; ALAVANJA *et al.*, 1987). Airborne dust from maize could also contain up to 206 ng aflatoxins g⁻¹, giving concentrations up to 107 ng m⁻³ air with 5–17% of particles smaller than 7 µm (BURG

et al., 1981, 1982; BURG and SHOTWELL, 1984). A role has also been postulated for tremorgenic mycotoxins produced by *A. fumigatus* in the allergic alveolitis of Swedish woodtrimmers although the presence of the toxin in spores still has to be demonstrated (LAND *et al.*, 1987). A toxicosis produced by inhalation of trichothecenes in spores of *Stachybotrys atra* has also been reported (CROFT *et al.*, 1986).

CONCLUSION

Occupational exposure to fungal spores is not a new phenomenon. Even early in the 18th century, RAMAZZINI (1713) could describe how threshers, sifters and measurers of grain were plagued by the dust, especially from heated and crumbling grain, with symptoms closely resembling allergic alveolitis. Such occupational exposure occurs widely in agriculture and is now recognized in many other industries, especially where stored products are handled. However, in the future there will need to be greater awareness of the opportunities for exposure and of occupational respiratory disease during biotechnological processes.

There are currently no threshold limit values applied to fungal and actinomycete spores and if these are to be derived there will need to be adequate sampling methods and a greater understanding of the dose-response relationships in occupational respiratory diseases and of the effects of constitutional factors in the exposed population. The suitability of different microbiological sampling methods has been reviewed by CROOK *et al.* (1988b) while REED *et al.* (1986) and TOPPING (1988) have described immunochemical methods for detecting airborne allergens. Such methods can be used to detect the presence even of unknown allergens in the atmosphere of relevance in outbreaks of occupational lung disease. They can also be used to assay known allergens and assess control measures. However, greater sensitivity is required to enable allergens to be detected in low volume personal samples to estimate individual workers exposure.

The control of airborne spores is best achieved at source firstly by good storage conditions and adequate drying for stored products or by the prevention of aerosols in biotechnological processes. If release of spores or aerosols is unavoidable, ventilation is required as close as possible to the point of release to prevent dispersal throughout the work environment. Personal exposure may be limited by suitable respiratory protection efficient against spores down to 1 μm diameter (LACEY *et al.*, 1982). Air conditioning systems present special problems. The accumulation of dirt and stagnant water needs to be avoided and the whole system maintained to a high degree of cleanliness with frequent steam cleaning or disinfection.

REFERENCES

- ALAVANJA, M. C. R., MALKER, H. and HAYES, R. B. (1987) Occupational cancer risk associated with the storage and bulk handling of agricultural foodstuff. *J. Toxicol. environ. Hlth* **22**, 247-254.
- AUSTWICK, P. K. C. (1982) Humidifier fever—a mycologist's nightmare. *Proc. 8th Cong., Int. Soc. Human Animal Mycol.* (Edited by BAXTER, M.), pp. 376-377.
- AUSTWICK, P. K. C., DAVIES, P. S., COOK, C. P. and PICKERING, C. A. C. (1986) Comparative microbiological studies in humidifier fever. In *Maladies des Climatiseurs et des Humidificateurs* (Edited by MOLINA, C.). *Colloque INSERM* **135**, 155-164.
- AVILA, R. and LACEY, J. (1974) The role of *Penicillium frequentans* in suberosis. Respiratory disease in workers in the cork industry. *Clin. Allergy* **4**, 109-117.

- BANASZAK, E. F., THIEDE, W. H. and FINK, J. N. (1970) Hypersensitivity pneumonitis due to contamination of an air conditioner. *New Engl. J. Med.* **283**, 271–276.
- BARROWCLIFF, D. F. and ARBLASTER, P. G. (1968) Farmer's lung: a study of an early acute fatal case. *Thorax* **23**, 490–500.
- BARUAH, H. K. (1961) The air spora of a cowshed. *J. gen. Microbiol.* **25**, 483–491.
- BAUR, X., FRUHMANN, G., HAUG, B., RASCHE, B., REIHER, W. and WEISS, W. (1986) Role of *Aspergillus* amylase in baker's asthma. *Lancet* **i**, 43.
- BELIN, L. (1980) Clinical and immunological data on "wood trimmer's disease" in Sweden. *Eur. J. resp. Dis.* **61**, suppl. 107, 169–176.
- BELIN, L. (1985) Health problems caused by actinomycetes and moulds in the industrial environment. In *Proceedings: Postgraduate Course, Sources of Allergens, June 5, 1984, Turku, Finland* (Edited by KOIVIKKO, A. and LOWENSTEIN, H.). *Allergy* **40**, suppl. 3, 24–29.
- BELIN, L. (1987) Sawmill alveolitis in Sweden. *Int. Archs Allergy appl. Immun.* **82**, 440–443.
- BERNSTEIN, R. S., SORENSEN, W. G., GARABRANT, D., REAUX, C. and TREITMAN, R. D. (1983) Exposure to respirable, airborne *Penicillium* from a contaminated ventilation system: clinical, environmental and epidemiological aspects. *Am. ind. Hyg. Ass. J.* **44**, 161–169.
- BLACKBURN, C. R. B. and GREEN, W. F. (1974) Extrinsic allergic alveolitis induced in the guinea-pig with *Streptomyces olivaceus*. *Clin. Allergy* **4**, 87–93.
- BOUTIN, P., TORRE, M. and MOLINE, J. (1987) Bacterial and fungal atmospheric contamination at refuse composting plants: a preliminary study. In *Compost: Production, Quality and Use* (Edited by DE BERTOLDI, M., FERRANTI, M. P., L'HERMITE, P. and ZUCCONI, F.), pp. 266–275. London, Elsevier.
- BROUWER, R., BIERSTEKER, K., BONGERS, P., REMIJN, B. and HOUTHUIS, D. (1986) Respiratory symptoms, lung function and IgG4 levels against pig antigens in a sample of Dutch pig farmers. *Am. J. ind. Med.* **10**, 283–285.
- BURG, W. R. and SHOTWELL, O. L. (1984) Aflatoxin levels in airborne dust generated from contaminated corn during harvest and at an elevator in 1980. *J. Ass. off. anal. Chem.* **67**, 309–312.
- BURG, W. R., SHOTWELL, O. L. and SALTZMAN, B. E. (1981) Measurements of airborne aflatoxins during the handling of contaminated corn. *Am. ind. Hyg. Ass. J.* **42**, 1–11.
- BURG, W. R., SHOTWELL, O. L. and SALTZMAN, B. E. (1982) Measurements of airborne aflatoxins during the handling of 1979 contaminated corn. *Am. ind. Hyg. Ass. J.* **43**, 580–586.
- BURGE, H. A. (1985) Fungus allergens. *Clin. Rev. Allergy* **3**, 319–329.
- BURGE, H. A., CHATIGNY, M., FEELEY, J., KREISS, K., MOREY, P., OTTEN, J. and PETERSON, K. (1987) Guidelines for assessment and sampling of saprophytic bioaerosols in the indoor environment. *Appl. ind. Hyg.* **3**, R10–R16.
- BUTCHER, B. T. and SALVAGGIO, J. E. (1986) Occupational asthma. *J. Allergy clin. Immun.* **78**, 547–556.
- CADHAM, F. T. (1924) Asthma due to grain rusts. *J. Am. Med. Ass.* **83**, 27.
- CLARK, C. S., RYLANDER, R. and LARSSON, L. (1983) Airborne bacteria, endotoxin and fungi in dust in poultry and swine confinement buildings. *Am. ind. Hyg. Ass. J.* **44**, 537–541.
- COHEN, H. I., MERIGAN, T. C., KOSEK, J. C. and ELDRIDGE, F. (1967) Sequoiosis: a granulomatous pneumonitis associated with redwood sawdust inhalation. *Am. J. Med.* **43**, 785–794.
- CORMIER, Y., BÉLANGER, J. and DURAND, P. (1985) Factors influencing the development of serum precipitins to farmer's lung antigen in Quebec dairy farmers. *Thorax* **40**, 138–142.
- CORNILLON, J., TOURAINE, J.-L., BERNARD, J.-P., LESTERLIN, P. and TOURAINE, R. (1975) Manifestations asthmatiques chez des ouvriers préparants des protéines alimentaires dérivées du pétrole (Allergie à *Candida tropicalis*?). [Asthmatic symptoms in workers preparing proteins for food from mineral oil.] *Rev. Fr. Allerg. Immun. Clin.* **16**, 17–23.
- CROFT, W. A., JARVIS, B. B. and YATAWARA, C. S. (1986) Airborne outbreak of trichothecene toxicosis. *Atmos. Environ.* **20**, 549–552.
- CROOK, B., BARDOS, P. and LACEY, J. (1988a) Domestic waste composting plants as sources of airborne micro-organisms. In *Aerosols: Their Generation, Behaviour and Application, Aerosol Society Second Conference* (Edited by GRIFFITHS, W. D.), pp. 63–68. Aerosol Society, London.
- CROOK, B., GRIFFIN, P., TOPPING, M. D. and LACEY, J. (1988b) An appraisal of methods for sampling aerosols implicated as causes of work-related respiratory symptoms. In *Aerosols: Their Generation, Behaviour and Application, Aerosol Society Second Conference* (Edited by GRIFFITHS, W. D.), pp. 327–333. Aerosol Society, London.
- CROOK, B., LACEY, J. and TOPPING, M. D. (1988c) Airborne dust and micro-organisms in a green coffee bean storage and handling warehouse. In *Aerosols: Their Generation, Behaviour and Application, Aerosol Society Second Conference* (Edited by GRIFFITHS, W. D.), pp. 353–357. Aerosol Society, London.
- CROOK, B., VENABLES, K. M., LACEY, J., MUSK, A. W. and NEWMAN TAYLOR, A. J. (1988d) Dust exposure and respiratory symptoms in a U.K. bakery. In *Aerosols: Their Generation, Behaviour and Application, Aerosol Society Second Conference* (Edited by GRIFFITHS, W. D.), pp. 341–345. Aerosol Society, London.

- CUTHBERT, O. D., BROSTOFF, J., WRAITH, D. G. and BRIGHTON, W. D. (1979) Barn allergy: asthma and rhinitis due to storage mites. *Clin. Allergy* 9, 229–236.
- DARKE, C. S., KNOWELDEN, J., LACEY, J. and WARD, A. M. (1976) Respiratory disease of workers harvesting grain. *Thorax* 31, 294–302.
- DAVIES, R. J., HENDRICK, D. J. and PEPYS, J. (1974) Asthma due to inhaled chemical agents: ampicillin, benzyl penicillin, 6 amino penicillanic acid and related substances. *Clin. Allergy* 4, 227–247.
- DE CLOSETS, F., NASTORG, C., DE BIÈVRE, C. and ROULLIER, A. (1985) Sensibilisations à *Aspergillus clavatus* découvert dans un élevage de lapins. [Sensitization to *Aspergillus clavatus* in a rabbit farm.] *Bull. Soc. Fr. Mycol. Méd.* 14, 315–319.
- DEGER, G. E. (1976) Aflatoxin—human colon carcinogenesis? [Letter.] *Ann. intern. Med.* 85, 204–205.
- DENNIS, C. A. R. (1973) Health hazards of grain storage. In *Grain Storage—Part of a System* (Edited by SINHA, R. C. and MUIR, W. E.), pp. 367–387. Avi Publishing Co., Westport, Connecticut.
- DE WECK, A. L., GUTERSOHN, J. and BÜTIKOFER, E. (1969) La maladie des laveurs de fromage ("Käsewascherkrankheit"): une forme particulière du syndrome de poumon du fermier. [Cheese-washer's disease: a particular type of farmer's lung syndrome.] *Schweiz med. Wschr.* 99, 872–876.
- DO PICO, G. A. (1986) Health effects of organic dusts in the farm environment. Report on diseases. *Am. J. ind. Med.* 10, 261–265.
- DONHAM, K. J., ZAVALA, D. C. and MERCHANT, J. A. (1984) Respiratory symptoms and lung function among workers in swine confinement buildings: a cross-sectional epidemiological study. *Arch. environ. Hlth* 39, 96–101.
- DUCHÉ, M. J. (1944) A propos du "Mal des Cannes de Provence". [Reed disease in Provence.] *Rec. Trav. Inst. natn. Hyg. (Paris)* 2, 242–252.
- DUNNER, L., HERMON, R. and BAGNALL, D. J. T. (1946) Pneumoconiosis in dockers dealing with grain and seeds. *Br. J. Radiol.* 19, 506–511.
- DVOŘÁČKOVÁ, I. (1976) Aflatoxin inhalation and alveolar cell carcinoma. *Br. med. J.* 1, 691.
- EATON, K. K., HENNESSY, T. J., SNODIN, D. J. and McNULTY, D. W. (1986) *Verticillium lecanii*. Allergological and toxicological studies on work exposed personnel. *Ann. occup. Hyg.* 30, 209–217.
- EDWARDS, J. H. (1986) The contribution of different microbes to the development of humidifier fever antigens. In *Maladies des Climatiseurs et des Humidificateurs* (Edited by MOLINA, C.). *Colloque INSERM* 135, 171–178.
- EDWARDS, J. H., GRIFFITHS, A. J. and MULLINS, J. (1976) Protozoa as sources of antigen in 'humidifier fever'. *Nature, Lond.* 264, 438–439.
- EMANUEL, D. A., LAWTON, B. R. and WENZEL, F. J. (1962) Maple-bark disease: pneumonitis due to *Coniosporium corticale*. *New Engl. J. Med.* 266, 333–337.
- EMANUEL, D. A., WENZEL, F. J. and LAWTON, B. R. (1975) Pulmonary mycotoxicosis. *Chest* 67, 293–297.
- FESTENSTEIN, G. N., LACEY, J., SKINNER, F. A., JENKINS, P. A. and PEPYS, J. (1965) Self-heating of hay and grain in Dewar flasks and the development of farmer's lung hay antigens. *J. gen. Microbiol.* 41, 389–407.
- FINNEGAN, M. J., PICKERING, C. A. C., DAVIES, P. S., AUSTWICK, P. K. C. and WARHURST, D. C. (1987) Amoebae and humidifier fever. *Clin. Allergy* 17, 235–242.
- FORSBECK, M. and EKENVALL, L. (1978) Respiratory hazards from proteolytic enzymes. [Letter.] *Lancet* ii, 524–525.
- GARFIELD, A., STONE, C., HOLMES, P. and TAI, E. (1984) *Serpula pinastri*—a wood decay fungus causing allergic alveolitis. *Aust. N.Z. J. Med.* 14, 4, suppl. 2, 552–553.
- GARI, M., LAUDAUD, F. and PINON, J. M. (1983) Asthme à *Penicillium candidum* avec présence de précipitines chez un ouvrier fromager. [Asthma due to *Penicillium candidum*, with precipitins present in a cheese worker.] *Bull. Soc. Fr. Mycol. Méd.* 12, 135–137.
- GÉRAULT, C., MORIN, O., DUPAS, D. and VERMEIL, C. (1984) Les alveolites allergiques extrinsèques dans l'industrie du fabrication des saucissons. [Extrinsic allergic alveolitis in the sausage-making industry.] *Arch. Mal. Prof. Méd. Tr.* 45, 608–610.
- GOODFELLOW, M., LACEY, J. and TODD, C. (1987) Numerical classification of thermophilic streptomycetes. *J. gen. Microbiol.* 133, 3135–3149.
- GRAVESEN, S. and JEPSEN, J. R. (1981) Luftfugtersyge. Et problem i den grafiske industri. [Extrinsic allergic alveolitis. A problem in the graphics industry.] *Ugeskr. Laeger* 143, 1211–1212.
- GREEN, W. F., HARVEY, H. P. B. and BLACKBURN, C. R. B. (1972) A shower curtain fungus (*Phoma violacea*) and allergic alveolitis. *Aust. N.Z. J. Med.* 2, 310.
- GREENE, J. G., TREUHAFT, M. W. and ARUSSELL, R. M. (1981) Hypersensitivity pneumonitis due to *Saccharomonospora viridis* diagnosed by inhalation challenge. *Ann. Allergy* 47, 449–452.
- GREGORY, P. H., LACEY, M. E., FESTENSTEIN, G. N. and SKINNER, F. A. (1963) Microbial and biochemical changes during the moulding of hay. *J. gen. Microbiol.* 33, 147–174.
- HARGREAVE, F. E., PEPYS, J. and HOLFORD-STREVEVS, V. (1968) Bagassosis. *Lancet* i, 619–620.
- HARRIES, M. G. and CROMWELL, O. (1982) Occupational asthma caused by allergy to pigs' urine. *Br. med. J.* 284, 867.

- HARRIES, M. G., LACEY, J., TEE, R. D., CAYLEY, G. R. and NEWMAN TAYLOR, A. J. (1985) *Didymella exitialis* and late summer asthma *Lancet* **i**, 1063–1066.
- HARRIS, L. H. (1939) Allergy to grain rusts and smuts. *Ann Allergy* **10**, 327–336.
- HEINONEN, O. P., HORSMANHEIMO, M., VOHLONEN, I. and TERHO, E. O. (1987) Prevalence of allergic symptoms in rural and urban populations. *Eur. J. resp. Dis.* **71**, suppl. 152, 64–69.
- HOŘEŠÍ, M., ŠACH, J., TOMŠIKOVÁ, A. and MECL, A. (1960) A syndrome resembling farmer's lung in workers inhaling spores of aspergillus and penicillia moulds. *Thorax* **15**, 212–217.
- HUUSKONEN, M. S., HUSMAN, K., JÄRVISALO, J., KORHONEN, O., KOTIMAA, M., KUUSELA, T., NORDMAN, H., ZITTING, A. and MÄNTYJÄRVI, R. (1984) Extrinsic allergic alveolitis in the tobacco industry. *Br. J. ind. Med.* **41**, 77–83.
- HYDE, H. A. (1972) Atmospheric pollen and spores in relation to allergy. I. *Clin. Allergy* **2**, 153–179.
- IZRAILET, L. I. and FEOKTISTOVA, R. P. (1970) Validation of sanitary zones for certain enzyme factories. *Gig. Sanit.* **35**, No. 6, 80–81 (in Russian).
- JACOBS, R. L., THORNER, R. E., HOLCOMB, J. R., SCHWIETZ, L. A. and JACOBS, F. O. (1986) Hypersensitivity pneumonitis caused by *Cladosporium* in an enclosed hot-tub area. *Ann. intern. Med.* **105**, 204–206.
- JIMINEZ-DIAZ, C., LAHOZ, C. and CANTO, G. (1947) The allergens of mill dust: asthma in millers, farmers and others. *Ann. Allergy* **5**, 519–525.
- KAGEN, S. L., FINK, J. N., SCHLUETER, D. P., KURUP, V. P. and FRUCHTMAN, R. B. (1981) *Streptomyces albus*: a new cause of hypersensitivity pneumonitis. *J. Allergy clin. Immun.* **68**, 295–299.
- KLAUSTERMEYER, W. B., BARDANA, E. J., JR. and HALE, F. C. (1977) Pulmonary hypersensitivity to *Alternaria* and *Aspergillus* in baker's asthma. *Clin. Allergy* **7**, 227–233.
- KONDO, T. (1969) Case of bronchial asthma caused by the spores of *Lentinus edodes* (Berg.) Sing. *Jap. J. Allergy* **18**, 81.
- KOTIMAA, M. H., HUSMAN, K. H., TERHO, E. O. and MUSTONEN, M. H. (1984) Airborne molds and actinomycetes in the work environment of farmer's lung patients in Finland. *Scand. J. Work Environ. Hlth* **10**, 115–119.
- KOTIMAA, M. H., TERHO, E. O. and HUSMAN, K. H. (1987) Airborne moulds and actinomycetes in the work environment of farmers. *Eur. J. resp. Dis.* **71**, suppl. 152, 91–100.
- KROIDL, R. F., AMTHOR, M., DÜRKES, U., FREITAG, V. and HAIN, E. (1984) Interstitielle Pneumonie durch Schimmelpilze aus einem Obstkühlhaus. [Interstitial pneumonia due to mildew in a cold storage depot for fruit.] *Prax. Klin. Pneumol.* **38**, 434–437.
- KURUP, V. P. (1984) Thermophilic actinomycetes: their role in hypersensitivity pneumonitis. In *Biological, Biochemical and Biomedical Aspects of Actinomycetes* (Edited by ORTIZ-ORTIZ, L., BOJALIL, L. F. and YAKOLEFF, V.), pp. 145–159. Academic Press, Orlando.
- KURUP, V. P., BARBORIAK, J. J. and SCRIBNER, G. (1976) Immunologic cross-reactions among thermophilic actinomycetes associated with hypersensitivity pneumonitis. *J. Allergy clin. Immun.* **57**, 417–421.
- KURUP, V. P., HOLLICK, G. E. and PAGAN, E. F. (1980) *Thermoactinomyces intermedius*: a new species of amylase negative thermophilic actinomycetes. *Science-Ciencia, Bol. Cient. Sur.* **7**, 104–108.
- KURUP, V. P., MÄNTYJÄRVI, R. A., TERHO, E. O., OJANEN, T. H. and KALBFLEISCH, J. H. (1987) Circulating IgG antibodies against fungal and actinomycete antigens in the sera of farmer's lung patients from different countries. *Mycopathologia* **98**, 91–99.
- LACEY, J. (1971a) *Thermoactinomyces sacchari* sp. nov., a thermophilic actinomycete causing bagassosis. *J. gen. Microbiol.* **66**, 327–338.
- LACEY, J. (1971b) The microbiology of moist barley storage in unsealed silos. *Ann. appl. Biol.* **69**, 187–212.
- LACEY, J. (1973a) Actinomycetes in soils, composts and fodders. In *Actinomycetales: Characteristics and Practical Importance* (Edited by SKINNER, F. A. and SYKES, G.), *Soc. appl. Bact. Symp. Ser.* No. 2, pp. 231–251. Academic Press, London.
- LACEY, J. (1973b) The air spora of a Portuguese cork factory. *Ann. occup. Hyg.* **16**, 223–230.
- LACEY, J. (1974) Moulding of sugar-cane bagasse and its prevention. *Ann. appl. Biol.* **76**, 63–76.
- LACEY, J. (1980a) The microflora of grain dusts. In *Occupational Pulmonary Disease—Focus on Grain Dust and Health* (Edited by DOSMAN, J. A. and COTTON, D. J.), pp. 417–440. Academic Press, New York.
- LACEY, J. (1980b) Colonization of damp organic substrates and spontaneous heating. In *Microbial Growth and Survival in Extremes of Environment* (Edited by GOULD, G. W. and CORRY, J. E. L.), *Soc. appl. Bact. Tech. Ser.* No. 15, pp. 53–70. Academic Press, London.
- LACEY, J. (1981) The aerobiology of conidial fungi. In *The Biology of Conidial Fungi* (Edited by COLE, G. T. and KENDRICK, W. B.), pp. 373–416. Academic Press, New York.
- LACEY, J. (1988a) Hazards to health from airborne spores in the mushroom industry. In *Aerosols: their Generation, Behaviour and Application, Aerosol Society Second Conference* (Edited by GRIFFITHS, W. D.), pp. 89–94. Aerosol Society, London.
- LACEY, J. (1988b) Actinomycetes as biodeteriogens and pollutants of the environment. In *Actinomycetes in Biotechnology* (Edited by GOODFELLOW, M., WILLIAMS, S. T. and MORDARSKI, M.), pp. 359–432. Academic Press, London.

- LACEY, J., HILL, S. T. and EDWARDS, M. A. (1980) Micro-organisms in stored grains: their enumeration and significance. *Trop. stored Prod. Inf.* **39**, 19–33.
- LACEY, J. and LACEY, M. E. (1964) Spore concentrations in the air of farm buildings. *Trans. Br. mycol. Soc.* **47**, 547–552.
- LACEY, J. and LACEY, M. E. (1987) Micro-organisms in the air of cotton mills. *Ann. occup. Hyg.* **31**, 1–19.
- LACEY, J. and MCLEAN, K. (1977) Combine cab comfort. *Power Eng* **56**, 11, 16–18.
- LACEY, J., NABB, S. and WEBSTER, B. T. (1982) Retention of actinomycete spores by respirator filters. *Ann. occup. Hyg.* **25**, 351–363.
- LACEY, J., PEPYS, J. and CROSS, T. (1972) Actinomycete and fungus spores in air as respiratory allergens. In *Safety in Microbiology* (Edited by SHAPTON, D. A. and BOARD, R. G.). *Soc. appl. Bact. Tech. Ser.* No. 6, pp. 151–184. Academic Press, London.
- LAND, C. J., HULT, K., FUCHS, R., HAGELBERG, S. and LUNDSTRÖM, H. (1987) Tremorgenic mycotoxins from *Aspergillus fumigatus* as a possible occupational health problem in sawmills. *Appl. environ. Microbiol.* **53**, 787–790.
- LANDER, F., JEPSEN, J. R. and GRAVESEN, S. (1985) Senastmatisk reaktion forårsaget af mikrosvampe i tobaksindustrien. [Late asthmatic reactions caused by microfungi in the tobacco industry.] *Ugeskr. Laeger* **147**, 2918–2919.
- LECOURS, R., LAVIOLETTE, M. and CORMIER, Y. (1986) Bronchoalveolar lavage in pulmonary mycotoxicosis (organic dust toxic syndrome). *Thorax* **41**, 924–926.
- LESKINEN, L. and KLEN, T. (1987) Storage mites in the work environment of farmers. *Eur. J. resp. Dis.* **71**, suppl. 152, 101–111.
- LIEBERT, C. A., HOOD, M. A., DECK, F. H., BISHOP, K. and FLAHERTY, D. K. (1984) Isolation and characterization of a new *Cytophaga* species implicated in a work-related lung disease. *Appl. environ. Microbiol.* **48**, 936–943.
- LONGBOTTOM, J. L. (1986) Antigen inter-relationships in outbreaks of humidifier fever. In *Maladies des Climatiseurs et des Humidificateurs* (Edited by MOLINA, C.). *Colloque INSERM* **135**, 165–170.
- LOSADA, E., HINOJOSA, M., MONEO, I., DOMINGUEZ, J., GÓMEZ, M. L. D. and IBÁÑEZ, M. D. (1986) Occupational asthma caused by cellulase. *J. Allergy Clin. Immun.* **77**, 635–639.
- MC SHARRY, C., ANDERSON, K. and BOYD, G. (1987) Serological and clinical investigation of humidifier fever. *Clin. Allergy* **17**, 15–22.
- MAIER, A., BRONNER, J., ORION, B., WISSLER, J. C. and HAMMANN, M. (1981) Bronchopneumopathies des ouvriers du bois et sensibilisation aux moisissures. [Bronchopneumopathies of wood workers and sensitization to moulds.] *Rev. Fr. Allerg.* **21**, 73–78.
- MILLNER, P. D., BASSETT, D. A. and MARSH, P. B. (1980) Dispersal of *Aspergillus fumigatus* from sewage sludge compost piles subjected to mechanical agitation in open air. *Appl. environ. Microbiol.* **39**, 1000–1009.
- MOLINA, C., AIACHE, J. M., BRUN, J. and CHEMINAT, J. C. (1971) Pneumopathies à précipitines. [Pneumopathies involving precipitins.] *Rev. Fr. Allerg.* **11**, 141–164.
- MOLINA, C., BEDU, M., JEANNERET, A., JOUANET, P., MOTTA, C. and DASTUGUE, B. (1982) Acquisitions récentes sur les alvéolites allergiques professionnelles. [Recent advances in occupational allergic alveolitis.] *Schweiz med. Wschr.* **112**, 192–197.
- MORIN, O., GÉRAULT, C., GARI, M., VERMEIL, C. and ETRILLARD, S. (1984) Manifestations allergique à *Penicillium* dans une usine de fabrication de saucissons. Étude clinique, sérologique, épidémiologique. [Manifestations of allergy to *Penicillium* in a factory making sausages.] *Bull. Soc. Fr. Mycol. Méd.* **13**, 403–407.
- NEWMAN TAYLOR, A. J. (1987) The lung and the work environment. In *Current Perspectives in the Immunology of Respiratory Disease* (Edited by KAY, A. B. and GOETZL, E. J.), pp. 55–67. Churchill Livingstone, Edinburgh.
- NICOLET, J., BANNERMAN, E. N., DE HALLER, R. and WANNER, M. (1977) Farmer's lung: immunological response to a group of extracellular enzymes of *Micropolyspora faeni*. An experimental and field study. *Clin. exp. Immun.* **27**, 401–406.
- OLIVIER, J. M., PICHOT, E., HOCQUET, P., OURY, M. and DURAND, R. (1975) Etude de la microflore fongique des champignonnières en fonction des postes de travail. [A study of fungal microflora of mushroom growers and its dependence on shifts worked.] *Bull. Soc. Fr. Mycol. Méd.* **4**, 65–67.
- PATTERSON, R., SOMMERS, H. and FINK, J. N. (1974) Farmer's lung following inhalation of *Aspergillus flavus* growing in mouldy corn. *Clin. Allergy* **4**, 79–86.
- PATTERSON, R., FINK, J. N., MILES, W. B., BASICH, J. E., SCHLEUTER, D. B., TINKELMAN, D. G. and ROBERTS, M. (1981) Hypersensitivity lung disease presumptively due to *Cephalosporium* in homes contaminated by sewage flooding or humidifier water. *J. Allergy clin. Immun.* **68**, 128–132.
- PAUWELS, R., DEVOS, M., CALLENS, L. and VAN DER STRAETEN, M. (1978). Respiratory hazards from proteolytic enzymes. [Letter.] *Lancet* **i**, 669.

- PEPYS, J. (1986) Occupational allergic lung disease caused by organic agents. *J. Allergy clin. Immun.* **78**, 1058–1062.
- PEPYS, J., JENKINS, P. A., FESTEINSTEIN, G. N., GREGORY, P. H., LACEY, M. E. and SKINNER, F. A. (1963) Farmer's lung: thermophilic actinomycetes as a source of 'farmer's lung hay' antigen. *Lancet* **ii**, 607–611.
- PICKERING, C. A. C., BATTEN, J. C. and PEPYS, J. (1972) Asthma due to inhaled wood dusts—Western red cedar and Iroko. *Clin. Allergy* **2**, 213–218.
- PICKERING, C. A. C., MOORE, W. K. S., LACEY, J., HOLFORD-STREVEVS, V. C. and PEPYS, J. (1976) Investigation of a respiratory disease associated with an air-conditioning system. *Clin. Allergy* **6**, 109–118.
- PRATT, D. S. and MAY, J. J. (1984) Feed-associated respiratory illness in farmers. *Arch. environ. Hlth* **39**, 43–48.
- PRATT, D. S., STALLONES, L., DARROW, D. and MAY, J. J. (1986) Acute respiratory illness associated with silo unloading. *Am. J. ind. Med.* **10**, 328.
- RAMAZZINI, B. (1713) *De morbis artificum diatriba*. [On the disease of occupation.] Translated by WRIGHT, W. C. Hafner, New York.
- REED, C. E., SWANSON, M. C. and YUNGINGER, J. W. (1986) Measurement of allergen concentration in the air as an aid in controlling exposure to aeroallergens. *J. Allergy clin. Immun.* **78**, 1028–1030.
- REVSBECK, P. and ANDERSEN, G. (1987) Storage mite allergy among grain elevator workers. *Allergy* **42**, 423–429.
- RHODY, J., BURRELL, R. J. and MORGAN, W. K. C. (1971) Yet another cause of allergic alveolitis. *Scand. J. resp. Dis.* **52**, 177–180.
- RIDDLE, H. F. V., CHANNELL, S., BLYTH, W., WEIR, D. M., LLOYD, M., AMOS, W. M. G. and GRANT, I. W. B. (1968) Allergic alveolitis in a maltworker. *Thorax* **23**, 271–280.
- ROBERTS, R. C., NELLES, L. P., TREUHAFT, M. W. and MARX, J. J., JR. (1983) Isolation and possible relevance of *Thermoactinomyces candidus* proteinases in farmer's lung disease. *Infect. Immun.* **40**, 553–562.
- RYLANDER, R. (1986) Lung diseases caused by organic dusts in the farm environment. *Am. J. ind. Med.* **10**, 221–227.
- RYLANDER, R. and HAGLIND, P. (1984) Airborne endotoxins and humidifier disease. *Clin. Allergy* **14**, 109–112.
- RYLANDER, R. and SNELLA, M.-C. (1976) Acute inhalation toxicity of cotton plant dusts. *Br. J. ind. Med.* **33**, 175–180.
- RYLANDER, R., HAGLAND, P., LUNDHOLM, M., MATTSBY, I. and STENQVIST, K. (1978) Humidifier fever and endotoxin exposure. *Clin. Allergy* **8**, 511–516.
- SAKULA, A. (1967). Mushroom worker's lung. *Br. med. J.* **3**, 708–710.
- SALKINOJA-SALONEN, M. S., HELANDER, I. and RYLANDER, R. (1982) Toxic bacterial dusts associated with plants. In *Bacteria and Plants* (Edited by RHODES-ROBERTS, M. and SKINNER, F. A.) *Soc. appl. Bact. Symp. Ser.* No. 10, pp. 219–233. Academic Press, London.
- SAMSON, R. A. (1985) Occurrence of moulds in modern living and working environments. *Eur. J. Epidemiol.* **1**, 54–61.
- SCHMITZ-SCHUMANN, M., COSTABEL, U., KREMPL-LAMBRECHT, L. and MATTHYS, H. (1986) Exogen allergic alveolitis (EAA) to mouldy wood (Abstract). *Third Int. Conf. Aerobiol.*, Basel, Switzerland, p. 95.
- SCHULZ, K. H., HAUSEN, B. M. and NOSTER, U. (1974) Allergy to spores of *Pleurotus florida*. [Letter.] *Lancet* **i**, 625.
- SOLLEY, G. O. and HYATT, R. E. (1980) Hypersensitivity pneumonitis induced by *Penicillium* species. *J. Allergy clin. Immun.* **65**, 65–70.
- SOLOMON, W. R. (1974) Fungus aerosols arising from cold-mist vaporizers. *J. Allergy clin. Immun.* **54**, 222–228.
- STALLYBRASS, F. C. (1961) A study of *Aspergillus* spores in the atmosphere of a modern mill. *Br. J. ind. Med.* **18**, 41–46.
- STORMS, W. W. (1978) Occupational hypersensitivity lung disease. *J. occup. Med.* **20**, 823–824.
- SYMINGTON, I. S., KERR, J. W. and MCLEAN, D. A. (1981) Type I allergy in mushroom soup processors. *Clin. Allergy* **11**, 43–47.
- TEE, R. D. and NEWMAN TAYLOR, A. J. (1987) Fungal allergy at work. *Pract. Allergy Immun. (Canada)* **2**, 92–96.
- TERHO, E. O., HUSMAN, K., KOTIMAA, M. and SJÖBLOM, T. (1980) Extrinsic allergic alveolitis in a sawmill worker. A case report. *Scand. J. Work Environ. Hlth* **6**, 153–157.
- TERHO, E. O., HUSMAN, K. and VOHLONEN, I. (1987) Prevalence and incidence of chronic bronchitis and farmer's lung with respect to age, sex, atopy and smoking. *Eur. J. resp. Dis.* **71**, suppl. 152, 19–28.
- TERHO, E. O. and LACEY, J. (1979) Microbiological and serological studies of farmer's lung in Finland. *Clin. Allergy* **9**, 43–52.
- THEDELL, T. D., MULL, J. C. and OLENCHOCK, S. A. (1980) A brief report of gram-negative bacterial endotoxin levels in airborne and settled dust in animal confinement buildings. *Am. J. ind. Med.* **1**, 3–7.

- THÖRNQVIST, T. and LUNDSTRÖM, H. (1982) Health hazards caused by fungi in stored wood chips. *Forest Prod. J.* **32**, 29–32.
- TOCHIGI, T., NAKAZAWA, T., DOBASHI, K., INAZAWA, M., FUEKI, R. and KOBAYASHI, S. (1982) A case of hypersensitivity pneumonitis due to inhalation of spores of *Pholiota nameko*. *Jap. J. thoracic Dis.* **20**, 1026–1031.
- TOPPING, M. D. (1988) Detection and measurement of airborne allergens. In *Aerosols: Their Generation, Behaviour and Application, Aerosol Society Second Conference* (Edited by GRIFFITHS, W. D.), pp. 335–340. Aerosol Society, London.
- TOPPING, M. D., LACEY, J. and CROOK, B. (1989). Aeroallergens from biological material: sampling and measurement. *Ann. occup. Hyg.* (in preparation).
- TOPPING, M. D., SCARISBRICK, D. A., LUCZYNSKA, C. M., CLARKE, E. C. and SEATON, A. (1985) Clinical and immunological reactions to *Aspergillus niger* among workers at a biotechnology plant. *Br. J. ind. Med.* **42**, 312–318.
- TÖRÖK, M., DE WECK, A. L. and SCHERRER, M. (1981) Allergische Alveolitis infolge Verschimmelung der Schlafzimmerwand. [Allergic alveolitis resulting from mould on bedroom walls.] *Schweiz. med. Wschr.* **111**, 924–929.
- TRAVERS, S., CROOK, B. and LACEY, J. (1988) Micro-organisms and dust in pig houses in Aberdeenshire. In *Aerosols: Their Generation, Behaviour and Application, Aerosol Society Second Conference* (Edited by GRIFFITHS, W. D.), pp. 139–145. Aerosol Society, London.
- VALLERY-RADOT, P. and GIROUD, P. (1928) Sporomycose des pelletiers de grains. [Sporomycosis of workers shovelling grain.] *Bull. Mem. Soc. méd. Hôp., Paris* **52**, 1632–1645.
- VAN ASSENDELFT, A. H. W. (1985) Asthma due to contaminated humidifiers. *Thorax* **40**, 560.
- VAN ASSENDELFT, A. H. W., RAITIO, M. and TURKIA, V. (1985) Fuel chip-induced hypersensitivity pneumonitis caused by *Penicillium* species. *Chest* **87**, 394–396.
- VINCKEN, W. and ROELS, P. (1984) Hypersensitivity pneumonitis due to *Aspergillus fumigatus* in compost. *Thorax* **39**, 74–75.
- WALLENSTEIN, G., BERGMANN, I., REBOHLE, E., GEMEINHARDT, H. and THÜRMER, H. (1980) Berufliche Atemtraktkrankungen durch Schimmelpilze bei Getreidemüllern und Bäckern. [Occupational airway disease due to mould in grain-millers.] *Z. Erkrank. Atm.-Org.* **154**, 220–233.
- WENZEL, F. J. and EMANUEL, D. A. (1967) The epidemiology of maple bark disease. *Arch. environ. Hlth* **14**, 385–389.
- WILLIAMS, N., SKOULAS, A. and MERRIMAN, J. E. (1964) Exposure to grain dust. I. A survey of the effects. *J. occup. Med.* **6**, 319–329.
- WOLF, F. T. (1969) Observations on an outbreak of pulmonary aspergillosis. *Mycopath. Mycol. appl.* **38**, 359–361.
- YOCUM, M. W., SALTZMAN, A. R., STRONG, D. M., DONALDSON, J. C., WARD, G. W., WALSH, F. M., COBB, O. M. and ELLIOTT, R. C. (1976) Extrinsic allergic alveolitis after *Aspergillus fumigatus* inhalation: evidence of a Type IV immunologic pathogenesis. *Am. J. Med.* **61**, 939–945.
- ZACHARIAE, H., HECH-THOMSEN, J., WITMEUR, O. and WIDE, L. (1982) Detergent enzymes and occupational safety. *Allergy* **36**, 513–516.
- ZADRAZIL, F. (1974) *Pleurotus*-sporen als Allergene. [Pleurotus spores as allergens.] *Naturwissenschaften* **61**, 456–457.
- ZEITLER, M. H. (1986) Staub-, Keim-, und Schad-gasgehalt in der Pferdestallluft, unter besondere Berücksichtigung der FLH (Farmer's lung hay) -Antigene. [Dust, spores and harmful gases in the air of stables, with special consideration of farmer's lung.] *Tierärztl Umschau* **41**, 839–845.