Mushroom-worker's lung

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The description in 1961 by Pepys *et al.*[1] of serum precipitins against antigens in mouldy hay in patients with farmer's lung has been followed by an expanding appreciation of pulmonary syndromes believed to occur as hypersensitivity reactions in response to inhaled organic antigens. The postulated common pathogenesis with a precipitin-mediated Type III allergic reaction occurring in the alveoli and distal airways has led to the descriptive term "extrinsic allergic alveolitis", as proposed by Pepys.[2] The recognized syndromes have been reviewed by Rankin *et al.*[3] and by Pepys,[2] and include a condition referred to variably as mushroom-worker's lung, mushroom-picker's lung, and mushroom-worker's disease. Sakula[4] has described four cases of respiratory illness occurring in mushroom-workers in Sussex, England. Two of these showed the presence of serum precipitins against either *Micropolyspora faeni (Thermopolyspora polyspora)* or *Thermoactinomyces vulgaris (Micromonospora vulgaris)*, both of the Actinomycetales species of bacteria. These organisms have been shown by many authors[3, 5-9] to act as antigens in cases of farmer's lung, supposedly initiating hypersensitivity processes in pulmonary tissue. Bringhurst, Byrne and Gershon-Cohen,[10] in 1959, reported 16 cases of unusual respiratory illnesses in migratory mushroom-workers in Chester County, Pennsylvania. Although immunological studies were not performed at that time, the clinical pattern described is such that an allergic etiology appears likely. An additional non-medical notation[11] of respiratory symptoms in a group of mushroom-workers in Kent is also suggestive of an allergic component.

This paper reports respiratory illnesses believed to represent pulmonary hypersensitivity reactions, which occurred in two men employed in a large commercial mushroom-growing facility in eastern Canada.

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Commercial mushroom growing

Examination of the commercial mushroom-growing process is necessary for an understanding of the disease entity described in mushroom-workers and its likely close relation to the farmer's lung syndrome. The particular process followed at the place of employment of the patients reported in this paper will be described. The arbitrary division into stages is based on the changing nature of the mushroom-growing medium, known as compost.

Stage A: Compost is prepared outdoors by the mixing of horse manure, brewer's grain, hay and oat straw, plus gypsum and organic proteins as needed to achieve optimal protein content and a pH of 8 to 8.5. The compost is placed in piles six feet wide, five feet high, and 200 feet long, kept well watered, and turned mechanically every three to four days. Physical, chemical and biological changes (referred to as composting) take place over a period of several weeks, with spontaneous heat generation sufficient to achieve a temperature in the centre of the piles up to 175° F. This has been called phase I composting, or initial fermentation.

Stage B: Compost is transferred by truck to tiered platforms in windowless composting houses where additional degradation takes place. This is phase II composting, also known as peakheating, pasteurization or final fermentation. A compost temperature of 130 to 140° F. is usually spontaneously maintained for five or six days, followed by cooling, again spontaneous, and requiring a further five to eight days. Occasionally, during winter, the pasteurization must be induced by the short-term addition of live steam. The microflora of compost in this stage has been investigated by Fergus,[12] who has found an abundance of thermophilic and thermotolerant moulds and actinomycetes. The compost becomes covered with "fire-fang", a visible white coating formed owing to the heat-activated microbiological proliferation.

Stage C: Compost is again transferred, by truck, to the mushroom-growing houses. During transfer, spawning is performed, with the introduction of specially prepared mushroom mycelium into the compost. This transfer process is re-

ferred to as the refill operation. Compost is placed in tiered wooden trays, five feet wide and 75 feet long, with an aggregate surface area of 5000 square feet per growing house. Casing, the application of a thin earth cover to the beds, is then performed.

Stage D: The mushroom, *Agaricus bisporus*, grows in several successive crops or flushes, which are manually picked as each flush matures. This stage is a relatively cool and inactive one for the compost, except that early in the stage vigorous spawn growth promotes temperatures that, if not controlled, would often exceed the autotoxic temperature of 95° F.

Stage E: Exhaustion of the growing abilities of the mushroom beds is followed by steaming, during which the air temperature reaches about 190° F. and the compost interior at least 170° F. This maximal temperature is held for at least five hours. The "dead" compost is then removed within three days for disposal. This relatively sterile medium is subject to rapid reinfection by airborne microorganisms if it is not removed within this time.

The total process in its many stages, with the associated heat-stimulated bacteriological activity, can be viewed as providing a rich source of actinomycetes and true fungal organisms, etiologically incriminated in farmer's lung and similar syndromes.

Case Reports

Both patients were 29-year-old French Canadian males with previous histories of excellent general health. They were non-smokers, without significant past respiratory illnesses, and with no history of allergic phenomena. Each had worked, as a boy, on his father's farm, but with no history of unusual respiratory symptoms at that time, without known exposure to mouldy hay, and with no recent visit to the farm preceding their illnesses.

Table I lists symptoms reported as common in cases of mushroom-worker's lung[4, 10] and farmer's lung.[3, 6] The patients' symptoms are indicated with their severity approximately quantitated on a scale of 1+ to 4+.

TABLE I
Summary of patients' symptoms

Symptoms described as common in mushroom-worker's lung[4, 10] and farmer's lung[3, 6]	Case 1	Case 2
Dyspnea on exertion	++++	++++
General malaise	++++	++++
Weight loss	24 lb.	20 lb.
Headache	++++	+++
Myalgia	++	+++
Cough	0	++
Sputum	0	+
Chills and fever	99° F.	103° F.
Chest pain	+++	++
Upper abdominal pain	0	+

Estimated severity of symptoms quantitated 1+ to 4+.

Case 1

This patient had worked for eight years in a number of positions in mushroom production. For the 13 months before the onset of his illness he had been involved with Stage C, as described above, in particular the transfer of compost from composting houses to growing houses. In early February 1969, he noted the onset of myalgia and general malaise, and during the following week he had, as well, a severe and persistent bitemporal headache, bilateral aching nonpleuritic chest pain and shortness of breath on exertion. An early feature he noted was an amelioration of symptoms during periods of absence from his work, with a relapse on return. The symptoms progressed over a five-week period, to the point of dyspnea and cyanosis at rest, and in this time he lost 24 lbs. in weight. Treatment to that point had consisted of antibiotics, because of physical findings suggesting a pneumonitis. The chest radiograph taken at this time (Figs. 1 and 2) suggests combined interstitial and airspace disease.

Six days later, on March 17, 1969, the patient was admitted to the Royal Edward Chest Hospital, Montreal. He

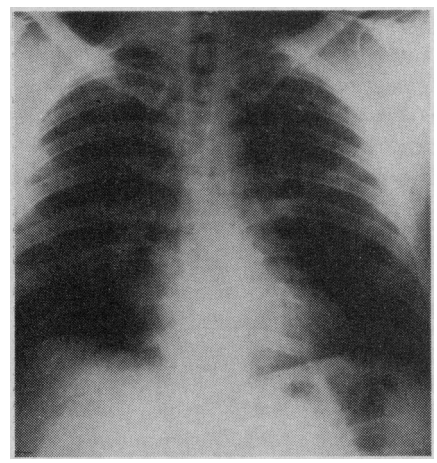

FIG. 1—Chest radiograph of Case 1, March 10, 1969, at peak of symptoms. Widespread, evenly distributed bilateral disease with a mixed reticular and acinar pattern suggesting combined interstitial and airspace disease.

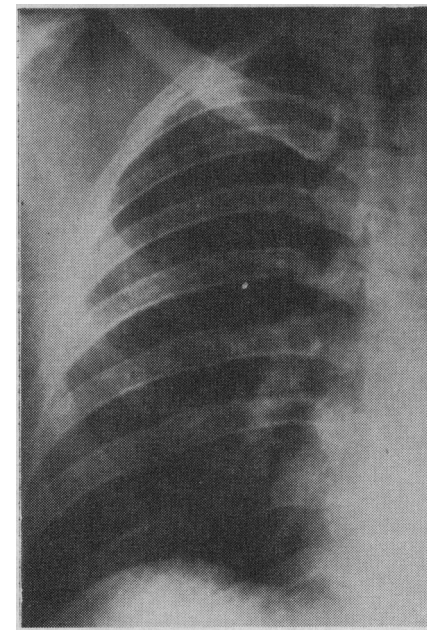

FIG. 2—Enlarged view of right lung field of radiograph in Fig. 1.

had not been at work for 10 days and had noted marked symptomatic improvement during his absence. The only symptoms remaining on admission were a mild headache and slight myalgia, and these disappeared within three days. He was afebrile on admission and remained so throughout the 11-day hospital course.

Physical examination on admission was unremarkable except for the coarse nature of the breath sounds. The chest radiograph, when compared to those taken a few days before, revealed clearing of the airspace involvement, leaving a predominantly reticular pattern. Discharge and subsequent follow-up chest radiographs were normal. The hemoglobin was 15 g. per 100 ml., ESR 2 mm. at the end of 1 hour, and leukocyte count 5900 per ml., with 59% mature neutrophils, 34% lymphocytes, 3% eosinophils and 4% monocytes.

Sputum cultures for fungi and for acid-fast bacilli were negative, while general cultures grew a normal respiratory flora. Sputa were induced with the aid of heated propylene glycol inhalations. Intradermal skin tests with old tuberculin 1/100, histoplasmin, blastomycin and coccidiomycin were negative. An aspergillin skin test was negative in both the immediate (5-40 minutes, reagin mediated) and intermediate (4-8 hours, precipitating antibody mediated) phases.

Serial pulmonary function and arterial blood gas results, including follow-up studies seven weeks after discharge, are summarized in Table II. The most significant abnormalities are the low pulmonary diffusing capacity for carbon monoxide and the admission hypoxemia, with progressive

return to normal oxygen levels.

Immunological investigation disclosed normal values for the serum immuno-electrophoresis, immunoglobulin quantitation, and beta-1-C serum complement levels. Agar gel double diffusion studies were performed to demonstrate precipitating antibodies in the patient's serum. These were negative with antigenic extracts of *Micropolyspora faeni, Thermoactinomycetes vulgaris* and *Aspergillus fumigatus.*

No therapy was administered during or following hospitalization. The patient was discharged in an improved condition and returned at once to work, but to a new position which eliminated contact with the mushroom compost in any of its stages. He has felt perfectly well since, without return of symptoms, and has regained the weight lost during the acute illness.

Case 2

This patient had been employed for two years as a compost leveller in Stage C of the mushroom-growing process. He noted the onset in early June 1968 of a non-productive cough, which was worse at work than during periods of absence. Additional symptoms appeared (Table I), and progressed in severity during the following five weeks. The patient eventually became short of breath on minimal exertion, was unable to continue work, and was admitted to another hospital on July 8, 1968.

Physical examination on admission revealed a tachypneic patient with an oral temperature of 101.4° F. and with bilateral rales throughout both lung fields but worse at the bases. He was not thought to be in heart failure. Hemoglobin was 15 g. per 100 ml. and leukocyte count 10,900 per ml., with 72% neutrophils, 15% lymphocytes, 6% monocytes, 3% eosinophils and 4% basophils. Sputum cultures for fungi and acid-fast bacilli were negative, while regular cultures grew a normal respiratory flora. The chest radiograph was normal. An antibiotic was prescribed. Rapid improvement followed, allowing discharge on the tenth hospital day with a diagnosis of bilateral bronchopneumonia.

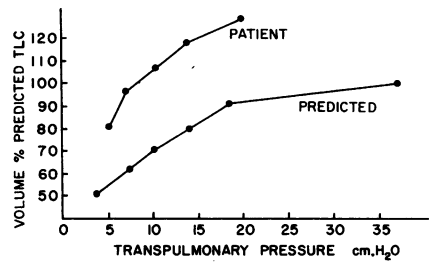

FIG. 3—Case 2. Respiratory mechanics pressure-volume curve.

The patient convalesced at home for approximately five weeks, without further therapy, after which he claimed he felt perfectly well, with normal exercise tolerance. Within four hours of his return to his old position, he experienced myalgia, general malaise and mild dyspnea on exertion. This progressed during the ensuing three hours to a state of near collapse and dyspnea at rest, so that urgent readmission to hospital was required.

The patient appeared acutely ill, and had diffuse bilateral inspiratory rales as well as some scattered rhonchi. Oral temperature was 99° F. The leukocyte count was 13,700 per ml., with 77% mature neutrophils, 16% juvenile neutrophils, 5% lymphocytes and 2% monocytes. A sputum culture grew *Streptococcus faecalis.* The chest radiograph was again within normal limits. Treatment with an antibiotic was reinstituted. He was discharged on the 15th hospital day with a diagnosis of bilateral bronchopneumonia.

Since return to work where he was given a different job, the patient has been well with the exception of a morning productive cough and decreased exercise tolerance only on extreme exertion.

The patient was admitted to the Royal Edward Chest Hospital in May 1969, nine months after the last acute symptoms. Physical examination was unremarkable, as were the bacteriological, biochemical and hematological investigations. The chest radiograph was normal. Skin tests with old tuberculin 1/100, histoplasmin, blastomycin and coccidiomycin were negative. Results of pulmonary function tests are shown in Table II and Fig. 3, with the principal abnormalities to be noted in the measurements of respiratory mechanics.

Immunological investigation revealed normal or negative results as noted in Case 1, except that serum precipitin studies were performed only for *Micropolyspora faeni* and *Aspergillus fumigatus.*

TABLE II
Pulmonary function and blood gas studies

		CASE 1 170.5 cm.				*CASE 2 162.5 cm.*	
		Predicted normal	*Mar. 18, 1969*	*Mar. 26, 1969*	*May 7, 1969*	*Predicted normal*	*May 9, 1969*
Vital capacity (l.)		4.65	4.05	4.25	4.70	4.51	4.70
Functional residual capacity (l.)		3.48	3.00	3.14	3.42	3.38	2.90
Residual volume (l.)		1.70	1.65	1.80	1.85	1.66	1.77
Total lung capacity (l.)		6.35	5.70	6.05	6.55	6.17	6.47
Timed vital capacity (% of VC)	1 sec.	83	72	78	89	83	73
	3 sec.	97	87	98	98	97	98
$D_{L,CO}$ (steady state) (ml. CO uptake/min./mm. Hg)							
Rest		22.3	13	15.6	12.4	21.9	17.8
Exercise: 300 Kpm		29.6	—	22.6	—	29	32.8
P_{aO_2} mm. Hg*			64	71	89		87
P_{aCO_2} mm. Hg			39	42	43		38
[H+] mμEq./l.			37.2	37.2	38		34.7
Resistance cm. H_2O/l./sec.		1–2		1.3		1–2	1.5
Maximum elastic recoil pressure		−35.5 cm. H_2O		−32		−35.5 cm. H_2O	−18
Static compliance l./cm. H_2O						.130	.280
Dynamic compliance l./cm. H_2O						(f = 10)	.415
						(f = 18)	.256
						(f = 35)	.332
f = respiratory frequency						(f = 52)	.216
						(f = 65)	.076

*Arterial blood gases. Patient breathing room air, at rest.
Kpm = Kilopond meters.

Discussion

The reported cases of the many variants of extrinsic allergic alveolitis, with the exception of farmer's lung, are so few in number that any discussion must rely heavily upon the existing information about the latter condition. Mushroom-worker's lung, apart from sharing a common immunological mechanism with farmer's lung, would seem likely to have a similar microbiological antigen source as well. Examination by Gregory and Lacey[13] of mouldy hay associated with farmer's lung revealed, in comparison with normal hay, a relative abundance of thermophilic moulds and actinomycetes. The ingredients of mushroom compost, including horse manure and hay, are also known to be rich sources of actinomycetes.[14] Fergus,[12] while studying mushroom compost during peakheating (see Stage B above), isolated 11 species of Acti-

nomycetales, as well as eight species of fungi, while at the same time cautioning that additional species likely remained undetected. The most common actinomycete isolated by Fergus was *Thermomonospora curvata*, while mouldy hay has generally yielded either *Micropolyspora faeni* or *Thermoactinomycetes vulgaris* as most frequent and abundant.[15, 16]

The reports of allergic alveolitis in a malt-worker secondary to the inhalation of the spores of *Aspergillus clavatus*,[17] and of maple-bark disease due to the spores of *Cryptostroma corticale*,[18] emphasize that non-actinomycetes can be the bacteriological source of antigenic material. There is some suggestion that even *Aspergillus fumigatus* can, with the proper conditions of exposure, lead to a farmer's-lung type of syndrome.[17] The causal implication of these relatively large fungal spores (up to 5 μ),[17] as compared to the small actinomycetes spores (0.5-1.3 μ),[15] suggests the potential etiological importance of the large numbers of fungal species isolated from mushroom compost,[12] in addition to the bacteria of the species Actinomycetales.

Those who work with mushroom compost are therefore exposed to a very large number of materials which potentially can be inhaled and act as antigens in the pulmonary tissue of susceptible individuals. Both reported patients worked with the compost during transfer from composting houses to growing houses, a process associated with much mechanical compost agitation. Bacterial and fungal retained particles would therefore have ample opportunity to become airborne, and so be available for inhalation. No studies of circulating particle numbers have been reported for mushroom compost, but Lacey and Lacey[19] have calculated the actinomycete spore content of the air within farm buildings to be as high as $1600 \times 10^6/m^3$. A man doing light work in this atmosphere is estimated to retain 0.75×10^6 spores per minute in his respiratory system.

Clinical course

The clinical course of farmer's lung has been well described.[3, 7, 9] Mushroom-worker's lung, as described in previous reports,[4, 10] would appear to fit a similar pattern. It is apparent that there is no completely typical course for either of these syndromes. The wide variations are likely due to differences in type and degree of exposure, and to individual variation in response, particularly as related to the modifying effects of antecedent or co-existing medical conditions. The cases reported in this paper would appear to fit well into the currently accepted spectrum of the allergic alveolitis syndromes.

Both patients were fortunate in that the nature and severity of their symptoms were such that recognition of the association between events at their place of work and their illnesses was possible. The clinical courses in these patients suggests a dominant hypersensitivity component. Early symptoms were noted to be alleviated during periods of absence from work, with a relapse upon return. The total relapse experienced by Case 2, beginning within four hours of return to work, and following complete recovery from the initial severe episode, supports the allergy concept. Hospitalization of Case 1, without therapy, effected clearing of symptoms, while Case 2 also appeared to benefit from isolation from his work. A toxic etiology is unlikely in view of the fact that these men were only two of approximately 100 employed at the same time in work which involved exposure to the mushroom compost. The medical officer of the company has no knowledge of similar illnesses during his 30 years in this capacity.

The identity of the causative antigen in these two cases remains to be established. The case histories strongly suggest a source in the mushroom compost during Stage C of the described process. The failure to demonstrate precipitating antibodies against the antigenic extracts listed suggests another microbiological source of the responsible antigen or antigens. The isolation of the many thermophilic organisms in mushroom compost requires special techniques[12] which were not available to the authors. Therefore the diagnosis of an allergic pulmonary reaction remains a presumptive one, and is based on a history of exposure to known sources of antigenic material, followed by a compatible clinical course.

Pulmonary function

There have been no reports of pulmonary function or arterial blood gases in mushroom-worker's lung. Farmer's lung, as well as other examples of extrinsic allergic alveolitis, must again be examined, to allow comparisons. Several contrasting patterns have been described, both in different series and within individual series. It is apparent that there is no single and completely characteristic pulmonary function abnormality in these syndromes. Only two dysfunctional patterns will be discussed in relation to the two cases described.

The most common pulmonary impairment reported is one characterized by a "stiff" non-compliant lung, with thickened alveolo-capillary membranes, and without significant abnormality in the conducting airways.[3, 20-22] The pulmonary diffusing capacity has been thought to be almost invariably decreased. Hypoxemia was seen to occur due to a diffusion defect, and also because of ventilation-perfusion (V/Q) abnormalities.

Case 1 could be interpreted as representative of this pattern, with the principal abnormalities the hypoxemia and the low $D_{L,CO}$. The serial vital capacity and lung volume studies, although not individually significantly abnormal, show a progression compatible with a resolving restrictive pulmonary pattern. For technical reasons full studies of respiratory mechanics are not available for this patient. The failure of the $D_{L,CO}$ to match improvement in other indices is in keeping with previous observations of the long delay in the return of this parameter to normal.[3, 23]

Note must be made of the time of pulmonary function study in these two patients. Case 2 was investigated nine months after his last acute symptoms, while Case 1 was first studied on the eleventh day after removal from his work and at a time when he had become almost asymptomatic. Several authors[3, 8] have noted that acute symptoms and many of the associated objective abnormalities change very rapidly in the initial

seven to 10 days after removal from antigenic exposure.

A second pulmonary function pattern has been described in some cases of extrinsic allergic alveolitis which includes evidence of important small airway obstruction.[21, 24] The functional observations can be supported by pathological evidence from lung biopsy of bronchiolitis obliterans.[6, 24-26] The failure of bronchiolar pathology to be reflected in conventional pulmonary function tests is understandable from the work of Macklem and his colleagues[27, 28] which establishes the relative contribution to airway resistance of central and peripheral airways. The distal airways are seen as normally providing only 25% of airway resistance, so that regular indices of airway obstruction may not fully reflect pathological events at that level.

Case 2 can be viewed as possibly representative of this second pattern of functional abnormality. The respiratory mechanics measurements showing normal airway resistance, markedly reduced maximal elastic recoil pressure, elevated static compliance and frequency dependence of the dynamic compliance can be interpreted as indicative of some form of small airway and alveolar disease. The preservation of the $D_{L,CO}$ most evident in the exercise study suggests that a process other than "conventional" pulmonary emphysema is involved.

The accumulated evidence suggests that the functional consequences of the alveolar allergic syndromes may be variable and complex, and that special investigative techniques may be required to fully define the physiological impairment. The presence of continuing functional abnormalities along with associated pulmonary disability, as reported in long-term follow-up studies of farmer's lung, emphasizes the serious consequences of these syndromes.[6-8]

Treatment

All authors agree that permanent removal from the antigen source is the single effective step, in allergic alveolitis, in preventing continuation or recurrence of symptoms. Corticosteroids have been reported as helpful in the treatment of acute episodes,[3, 6, 8, 22] although there have been no controlled studies. The use of steroids to suppress symptoms in the presence of continuing antigenic exposure appears hazardous, as there is no evidence that symptom suppression is associated with arrest of the pathological processes in pulmonary tissue. The wearing of face masks during periods of exposure has been advocated for both farmer's lung[9] and mushroom-worker's lung.[4] Others[29] emphasize the small size of the actinomycete spores (0.5-1.3 μ),[17] and question the efficiency of face masks in excluding these particles.

Quantitation of the efficiency of particle exclusion by protective masks has been the subject of a recent study.[30] A variety of commercially available respiratory protective devices were challenged with particles of different sizes and specific gravities. No mask tested completely excluded particles of mean size varying from 0.33 to 2.0 μ. Percentage particle penetration for devices approved under the United States Bureau of Mines Schedule 21B[31] ranged from 0.2% to 4.8%. Non-approved devices allowed up to 48% dust penetration. Exact knowledge of the size of offending particles and of the performance specifications of available protective masks is seen to be required. The likelihood of significant particle entry into the airway would appear high even with the continuous use of a properly fitting, appropriate mask.

One of the variables governing the severity of individual symptom episodes following antigenic exposure appears to be the intensity of the exposure.[17, 24, 29] Face masks, by reducing the inhaled antigen mass, might convert identifying symptoms to minimal or undetectable levels. Continuing occult pulmonary damage would be an unacceptable price for temporary symptom suppression. Great caution would therefore seem indicated in recommending masks for use in the allergic alveolitis syndromes.

The two patients discussed did not receive any specific treatment with the exception of a short period of antibiotic therapy in Case 2. Permanent removal from the presumed antigen source has been followed by a complete loss of symptoms. Both patients, however, show continuing pulmonary function abnormalities in the absence of symptoms and in the presence of normal chest radiographs.

The serum precipitin studies were performed by the Immuno-Pathology Laboratory, Royal Victoria Hospital, Montreal, Quebec.

ADDENDUM

Follow-up pulmonary function studies were performed in November 1969. Both patients had continued to avoid re-exposure to the mushroom compost, and were asymptomatic. Changes noted since the previous studies in May 1969 were: Case 1—resting and exercise diffusing capacities significantly improved. Case 2—changes in respiratory mechanics with the return to normal of the maximum elastic recoil pressure, and a moderate decrease in the static compliance.

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