

## Type III Hypersensitivity Reaction in Mushroom Growers

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*Some respiratory symptoms in mushroom growers such as mushroom worker's lung develop by inhalation of certain agents arising from the environment of mushroom cultivation. Recently we observed mushroom workers who had respiratory symptoms which might be type III hypersensitivity reaction to the antigen of *Pleurotus floridae*.*

*We gave questionnaires to all the mushroom growers at one of the biggest cultivation areas of mushrooms, *Pleurotus floridae* in Pocheon, Kyunggi Province. Those with respiratory symptoms were subjects for the study. CBC, chest X-ray, pulmonary function test, skin test with *Pleurotus floridae* extract, and precipitin antibody test to *Pleurotus floridae* were performed in the study subjects.*

*Out of a total 308 mushroom workers, 23 workers (14 males, 9 females) had respiratory symptoms. Their mean age was 45 years, and their mean duration of engagement was 3.4 years. Their main symptoms were cough (100%), sputum (82.6%), dyspnea (43.5%), and fever with chills (13.0%). Two cases showed increased interstitial lung markings on chest X-ray films. Sixteen cases (73.9%) showed precipitin antibodies against *P. floridae* extract by counterimmunoelectrophoresis. Antibodies against *Micropolyspora faeni* and *Thermoactinomyces vulgaris* were not detected in any subject.*

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**Key Words:** *Mushroom worker's lung, Hypersensitivity, *Pleurotus floridae*, Precipitin antibody*

## INTRODUCTION

Respiratory disorders can develop in mushroom growers by the inhalation of certain agents arising from the environment of mushroom cultivation houses<sup>1-4</sup>. Mushroom worker's lung is the most important disease among them and is an interstitial lung disease resulting from the immunological reaction to the antigens associated with the organic particles<sup>4</sup>. It is more common than ordinarily thought<sup>5</sup>. The causative agents are multiple, and new antigens are being identified continuously<sup>6-9</sup>.

As the commercial demand for mushrooms increases, many Korean farmers have been engaged in mushroom growing during the winter season after harvest. Recently we observed mushroom growers who had respiratory symptoms which might be type III hypersensitivity reaction to the antigen of mushroom, *Pleurotus floridae*, which was suggested as hypersensitivity pneumonitis. In this article we report the immunologic findings of those subjects with clinical characteristics.

## MATERIALS AND METHODS

There were 108 mushroom houses in one of the largest cultivation areas of *Pleurotus floridae* located in Pocheon, Kyeonggi Province, 68 km from Seoul, where approximately 308 people were engaged in mushroom growing in 1985. The

cultivation house was almost enclosed with a thick wall to protect it from direct sunlight and to insulate it in order to maintain a temperature of 15~20°C (Fig. 1). It usually had 8 small straw mats on each bed (Fig. 2) and produced numerous basidiospores from the gills of basidiocarps (Fig. 3). The spores were densely dispersed in the air so that the growers inhaled large amounts of basidiospores while they were harvesting mushrooms.

Among 308 mushroom growers, 23 (7.5%) of them (14 male, 9 female) had respiratory symptoms associated with mushroom cultivation (Table 1). Their mean age was 45 years and mean duration of engagement was 3.4 years.

Complete blood count, chest X-ray, and spirometry (FEV1 and flow volume curve) were checked. Skin tests were done by intradermal injection of 0.2 ml of *P. floridae* extract (100 mcg/ml). Fresh mushroom was homogenized with a blender in normal saline, and then the clear extract was separated from the mycelial debris by centrifugation at 10,000 rpm for 20 min. The criterion for a positive immediate skin test was a greater reaction than half of the histamine control (0.1 mg/ml). A positive 6-hr skin reaction was > 10 mm induration, and no induration or less than 10 mm was interpreted as negative. Immunodiffusion tests and immunoelectrophoresis were performed in order to detect precipitating antibodies to the *Pleurotus floridae* antigens in serum specimens collected from all subjects. Antigens of *Micropolyspora faenii*, *Thermoactinomyces vulgaris*, and the extracts of other edible mushrooms, *Lentinus*



Fig. 1. The cultivation house was almost totally enclosed with a thick wall to protect from direct sunlight and to insulate in order to maintain a temperature of 15~20°C.

## TYPE III HYPERSENSITIVITY REACTION IN MUSHROOM GROWERS

ebodes and *Flammulina velutipes*, were also included in this test. Agar gel plate was air-dried and stained with amidoblack (Fig. 4).

### RESULTS

The symptoms associated with mushroom culti-



Fig. 2. The interior of the cultivation house. There were 8 small straw beds to grow mushrooms.

vation are shown in Table 2. Cough was the most common symptom, and an increased amount of sputum was found in 19 subjects and dyspnea in 7 subjects. Three subjects complained of fever and chill. Complete blood counts were all normal and no eosinophilia seen. Spirometry was also normal in all subjects. Two cases showed slightly increased interstitial markings on chest X-ray (Fig. 5). Precipitating antibodies to *P. floridae* extracts were found in serum specimens of 16 subjects (Table 3). One to 4 precipitin bands were observed on the counterimmunoelectrophoresis plate. However, none had antibody to *M. faenii* and *T. vulgaris* which have been known to be common offending antigens in mushroom worker's lungs.

There was no reaction to the extracts of *L. ebodes* and *F. velutipes* so that it ruled out cross reactions with other edible mushrooms. Also, none of the normal subjects reacted to *P. floridae* antigen, suggesting that a positive precipitin reaction to this organism was closely associated with cultivation of this mushroom and related with its symptoms. Levels of total IgE were slightly higher in positive reactors than in negative, but it was not statistically significant.

On the intradermal skin tests, positive immediate reaction was observed in 7 subjects (30.4%) and late reaction in 13 subjects (56.5%) as seen in Table 5. The relationship of precipitating antibody and 6-hr skin reaction is shown in Table 6. Among 13 positive reactors, 11 subjects (84.6%) had precipitating antibodies to *P. floridae*, and 5 out of 10 negative reactors also had precipitating anti-



Fig. 3. Basidiocarps of *Pleurotus floridae*. Numerous basidiospores are produced from their gills.

**Table 1.** General Information on 23 Mushroom Growers with Respiratory Symptoms

Sex	Subjects	Mean Age	Mean Duration of Engagement
Male	14	44.4 ± 9.0	3.7 ± 2.4 (3 mo – 7 yr)
Female	9	46.9 ± 7.0	3.0 ± 1.3 (1 yr – 4 yr)
Total	23	45.0 ± 8.0	3.4 ± 2.1 (3 mo – 7 yr)

\* Total number of mushroom growers surveyed was 308.

**Table 2.** Symptoms Associated with Mushroom Cultivation

Symptoms	No. of Subjects	%
Cough	23	100.0
Sputum	19	82.6
Dyspnea	7	43.5
Fever and chill	3	13.0

**Table 3.** Counterimmunoelectrophoresis of Serum Specimen

Antigens	Symptomatics (23)	Controls (7)
<i>P. floridae</i>	16	0
<i>M. faenii</i>	0	0
<i>T. vulgaris</i>	0	0
<i>L. ebodes</i>	0	0
<i>F. velutipes</i>	0	0

**Table 4.** Clinical Data of Positive Reactors (16) to *P. floridae* on CIE

	Precipitating Antibody	
	Positive	Negative
Male	10	4
Female	6	3
Mean age (yr)	47.3 ± 10.3	39.8 ± 6.8
Mean duration of engagement (yr)	3.5 ± 2.3	3.3 ± 1.5
Total IgE (PRIST)	283.6 ± 2.9	169.7 ± 6.8

bodies.

## DISCUSSION

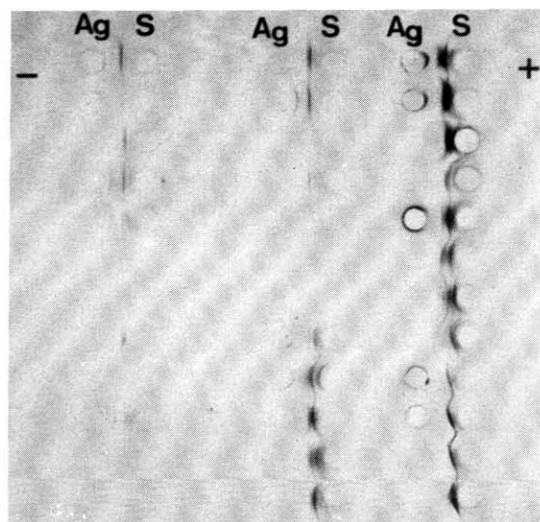
Since respiratory disorders due to dusts of

**Table 5.** Intradermal Skin Reactions to *P. floridae* Antigen

	Positive		Negative	
	No.	%	No.	%
Immediate reaction	7	30.4	16	69.6
Late reaction	13	56.5	10	34.8

**Table 6.** Relationship between Skin Reaction and Precipitating Antibodies

6-hr Skin Reaction	Precipitating Antibody	
	Positive	Negative
Positive	11	2
Negative	5	5



**Fig. 4.** Agar gel plate stained with amidoblack. Stained bands reveal positive reactions between the subject's serum and *P. floridae* extract.

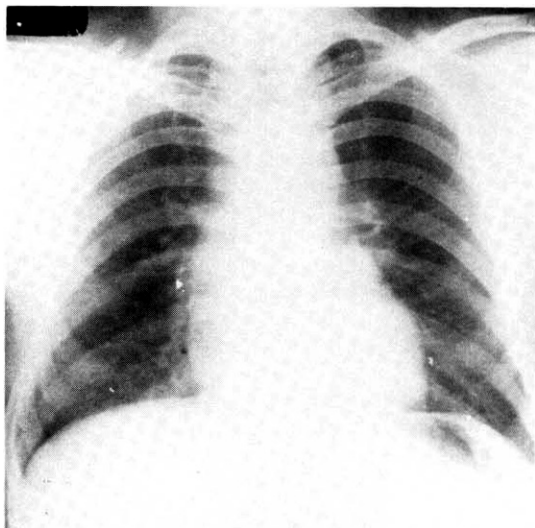


Fig. 5. This chest X-ray shows slightly increased interstitial markings in both lower lung fields in one subject.

vegetable origin had been described first by Ramanizzi (1713) in flax workers<sup>9</sup>, many similar conditions have been recognized<sup>10</sup>. Campbell described those symptoms as farmer's lung in 1932<sup>11</sup>, and now it has been known as a not infrequent condition occurring in agricultural workers who are often exposed to dusts arising from moldy forage and vegetable matter.

Farmer's lung may be an industrial lung disease due to hypersensitivity to an antigen arising from the dust of moldy forage. Since Pepys et al. (1963) reported that the major antigens involved were the spores of thermophilic actinomycetes growing in the heated hay, a wide variety of organic dusts<sup>12</sup> and chemicals has been identified as the causative agents, and new offending agents have come to be known continuously.

Mushroom worker's lung is one type of farmer's lung occurring in mushroom growers. Mushrooms were first grown commercially shortly after the American Civil War. In Korea edible mushroom cultivation has been profitable, so that the number of mushroom growers has recently increased. The most popular species of mushroom is *P. floridae*, and it grows from November to February during the winter season after harvest. Mushrooms are harvested 2 or 3 times a season.

We observed 23 individuals, who have had respiratory symptoms, out of the 308 mushroom growers in the Pochen area, one of the largest *P.*

*floridae* cultivation areas (Table 1). Incidence was quite high, and cough and increased sputum were the most common symptoms (Table 2). CBC and spirometry were normal, and chest X-ray revealed an abnormality in only 2 subjects. It was thought that abnormal laboratory findings could not be found because they were checked after cultivation season.

The 16 subjects (69.9%) had precipitin bands to *P. floridae* extracts by CIEP (Table 3). They did not react to actinomycetes antigens, which were the most frequent cause of farmer's lung, and also to other mushroom antigens and no control subjects reacted to *P. floridae* antigen. All this evidence suggests that their symptoms might have resulted from the exposure to *P. floridae*, but it cannot be ruled out that some of them were nonspecific or irritant-induced.

Pepys and Jenkins obtained positive reactions in 91% of the patients with farmer's lung by the double-diffusion test and in 89% in the immunoelectrophoretic test<sup>13</sup>. Freedman et al. detected precipitating antibody in 61.3% of the patients with farmer's lung<sup>14</sup>, and ELISA detected antibodies in 77.4% of the cases. Our result, that precipitating antibody was positive in 69.9% by CIEP (Table 3), is similar to that of Freedman et al. but slightly lower than that of Pepys and Jenkins. Approximately 8% to 10% of healthy farmers have circulating antibodies to antigens of causative organisms of farmer's lung<sup>14</sup>. So it might be possible that some of them in our study had nonspecific or irritant-induced respiratory symptoms.

The existence of type III hypersensitivity reaction may be confirmed by 6-hr skin tests<sup>14</sup>. A positive 6-hr late skin reaction was observed in 13 (56.5%) cases in this study, and late reaction was observed in 11 (68.8%) out of 16 precipitin positive reactors. This result was comparable with Freedman's finding (71%). Hypersensitivity pneumonitis is mainly involved by the mechanism of the type III hypersensitivity reaction<sup>15,16</sup>, but some patients with hypersensitivity pneumonitis may have type I allergic reaction<sup>17</sup>. Intradermal skin tests revealed that 7 (30.4%) out of 23 subjects showed an immediate reaction in our study. This result was slightly lower than that of Freedman et al. (58%) but higher than that of Pepys and Jenkins (18%). The mechanism of type I reaction in hypersensitivity pneumonitis will be further studied.

In one of the mushroom cultivation areas in Korea, 23 individuals out of 308 mushroom growers had respiratory symptoms which were

suggestive of hypersensitivity pneumonitis due to frequent heavy exposure to *P. floridae* basidiospores during cultivation and harvest. Their precipitin antibody and skin reactions to *P. floridae* antigen were compatible with such a presumptive diagnosis. However, further studies are required to confirm the diagnosis including lung biopsy and provocation test with inhalation challenge.

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