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Allergic Bronchopulmonary Aspergillosis in a Cane-Sugar Mill

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Allergic bronchopulmonary aspergillosis is reported in two (1.5 %) of 131 workers occupationally exposed to *Aspergillus fumigatus* at the U.D. Sugar Mills, Shamli. Twelve of the workers revealed Type I (9.2 %) and three (2.8 %) Type III skin hypersensitivity against the fungus. Serum precipitins were demonstrated in two out of 44 workers and positive sputum cultures in 26 out of 58 workers. It is suggested that constitutional predisposition of the host may be a more important factor than the extent of exposure to the fungus in the development of allergic bronchopulmonary aspergillosis.

Key words: aspergillosis – *Aspergillus fumigatus* – hypersensitivity, imediate – hypersensitivity, delayed – skin tests – precipitins

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In a separate paper we have reported on the special association of *Aspergillus fumigatus* with sugar-cane bagasse and the aerial preponderance of this species in sugar mills near Delhi (Sandhu et al. 1976). It seemed obvious that the employees of the mills, especially those engaged in the shifting or feeding of bagasse under the boilers as fuel, were occupationally exposed to inhalations of a large number of *A. fumigatus* spores. The well-known pathogenic and allergenic potential of *A. fumigatus* (Pepys et al. 1959, Henderson 1968, Emmons et al. 1970, Pena 1971, Khan et al. 1976) prompted us to probe the clinical significance of this recurrent exposure to the fungus.

SUBJECTS AND METHODS

The study was carried out on a sample of 163 industrial workers, 131 of whom worked at the Upper Doab Sugar Mills, Shamli (U.P.), situated about 90 km north east of Delhi, and 32 at the Ballarpur Paper Mills, Jagadhri (Haryana), located about 200 km north of Delhi. The subjects investigated at Shamli worked in the following sections of the sugar mill: boiler room (66), drier room (8), pan room (7), crusher room (6), baling room (6) and miscellaneous sections (38). These workers were divided into two groups. Group I comprised 30 workers with chronic respiratory symptoms. On the basis of their history, symptomatology and previous in-

vestigations, these workers could broadly be classified into the following categories: bronchial asthma (13), chronic bronchitis (11), allergic bronchitis (4), and pulmonary tuberculosis (2). Group II comprised 101 workers who were either asymptomatic or had only minor respiratory complaints of short duration. Of the 32 workers examined from the Ballarpur Paper Mills, five had chronic cough and breathlessness, and four had cough alone. As controls, 28 healthy volunteers from the Staff of V.P. Chest Institute Delhi, were also investigated. All the subjects were skin tested with aspergillin. A 2 + or higher reaction read in terms of induration and erythema after 20 min and an oedematous swelling exceeding 30 mm in diameter after 6–8 h of the intracutaneous test was taken as positive for Type I and III hypersensitivity. Further tests were done mostly on positive reactors or those workers who had respiratory affections. These tests include eosinophil counts in sputum and peripheral blood, immunodiffusion test against antigens of *A. fumigatus, A. flavus* and *A. niger,* and culture of sputum. Details of procedures for the foregoing tests have been described elsewhere (Khan et al. 1976). The diagnosis of allergic bronchopulmonary aspergillosis was based on the following criteria: (a) extrinsic asthma with history of episodic attacks of breathlessness, (b) dual hypersensitivity response to skin test with aspergillin, (c) moderate blood eosinophilia with an absolute count of more than 500 cells/mm^3, (d) presence of *A. fumigatus* in sputum or sputum plug, (e) precipitin band against *A. fumigatus* in immunodiffusion test and (f) pulmonary infiltrations in chest skiagrams. No attempt was made to carry out thorough investigations of those workers who apparently suffered from diseases other than bronchopulmonary aspergillosis as indicated by negative dual skin reaction and lack of precipitins, and other features associated with allergic bronchopulmonary aspergillosis.

RESULTS

The results of the study are presented in Tables 1–2. *Aspergillus fumigatus* was iso-

TABLE 1. *Results of laboratory investigations on 163 workers examined for allergic bronchopulmonary aspergillosis (ABPA).*

	U.D. Sugar Mills, Shamli		Ballarpur Paper Mills, Jagadhri
	Group I	Group II	
No. workers investigated	30	101	32
Skin hypersensitivity to *A. fumigatus*			
Type I	7 (23.3 %)	5 (5.0 %)	3 (9.3 %)
Type III	3 (10.0 %)	0	1 (3.1 %)
Serum precipitins	2 (6.6 %)	0/14	ND
A. fumigatus in sputum	8	18/*28	3/*10
Blood eosinophils > 10 %	8	3/14	ND
No. patients with ABPA	2 (6.6 %)	0	0

* Number positive / Number of patients tested. ND – Not done.

TABLE 2. *Results of laboratory investigations and some relevant details concerning 12 workers from U.D. Sugar Mills, Shamli, with Type I skin hypersensitivity to* Aspergillus fumigatus.

Case no.	Age and sex	Place of work	Duration of work (years)	History of illness* (years)	Provisional† diagnosis	Blood eosinophils %	*Aspergillus fumigatus*			
							Skin reaction Type I	Skin reaction Type III	Precipitins	Culture
** 1	47, M	Not fixed	18	5	BA	18	+	+	+	+
** 2	50, M	Boiler room	20	8	BA	21	+	+	+	+
3	37, M	Crusher room	8	12	AB	10	+	–	–	–
4	52, M	Pan room	18	6	BA	13	+	+	–	–
5	40, M	Not fixed	3	2	BA	7	+	–	–	+
6	30, M	Boiler room	12	3	BA	15	+	–	–	–
7	50, M	Boiler room	2	4	BA	13	+	–	–	+
8	22, M	Boiler room	4	–	–	10	+	–	–	–
9	40, M	Boiler room	15	–	–	13	+	–	–	–
10	52, M	Boiler room	30	–	–	4	+	–	–	+
11	45, M	Boiler room	15	–	–	6	+	–	–	–
12	38, M	Crusher room	8	–	–	3	+	–	–	–

* Attacks of breathlessness, cough and expectoration.
** Diagnosed as cases of allergic bronchopulmonary aspergillosis.
† BA – Bronchial asthma. AB – Asthmatic bronchitis.

lated at the first trial from sputum in 26 (44.8 %) of the 58 workers from U.D. Sugar Mills, Shamli who were most exposed to the fungus from the heavily laden environment of the mill. Type I skin hypersensitivity to *A. fumigatus* was recorded in 12 cases (Table 2). Of these, seven belonged to group I and had complaints of cough, expectoration and breathlessness with history of allergic rhinitis in four of them and smoking in three. Three workers belonging to group I had dual skin reaction and two of them revealed 1–2 precipitin bands specific against *A. fumigatus* antigens in the immunodiffusion test (Fig. 1). A diagnosis of allergic bronchopulmonary aspergillosis was further confirmed in these two cases by demonstration of a moderate rise in blood eosinophils (10–20 %), positive sputum cultures, and pulmonary infiltrations. A detailed case re-

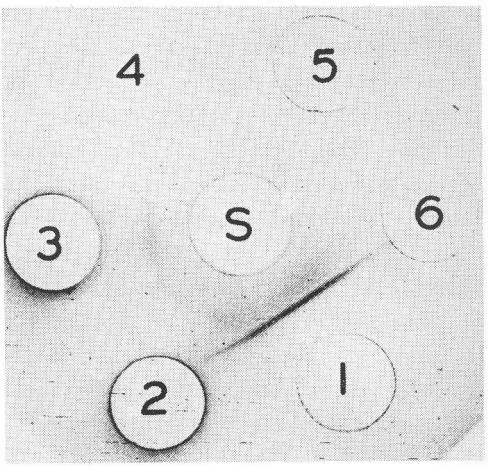

Figure 1. Double diffusion test with concentrated serum (3 ×) of Case 2 in central well 'S'. The peripheral wells contain different antigens: well 1, *A. fumigatus* strain isolated from Case 2; wells 2 and 3, two other strains of the species; wells 4 and 5, *A. flavus;* well 6, *A. niger.* Note a strong band opposite well 1 and weak identical bands against wells 2 and 3.

port on Case 1 has already been published (Case 4, Sandhu et al. 1972).

The immunodiffusion tests were uniformly negative against the three species of *Aspergillus* in all the other sera tested. The criteria for diagnosis of allergic bronchopulmonary aspergillosis were not fulfilled in any of the remaining workers with Type I skin hypersensitivity, nor in the worker from Ballarpur Paper Mills who had a Type III reaction. The 28 healthy controls yielded negative results for skin hypersensitivity, precipitins and culture of oropharyngeal washings for *A. fumigatus*.

DISCUSSION

It has been discussed from time to time that aspergillosis could be an occupational disease (Renon 1897, Yesner & Hurwitz 1950, Strelling et al. 1966, Henderson 1968) but supporting epidemiologic evidence is lacking. The present study, although limited in scope, suggests that persistent exposure to high concentrations of *A. fumigatus* may not lead to marked sensitization and development of allergic bronchopulmonary aspergillosis unless the subject is inherently predisposed to the disease. Immediate, Type I skin hypersensitivity to *A. fumigatus* was recorded in 9.2 % of the subjects and was considerably higher in group I which comprised workers with chronic respiratory complaints. Although immediate-type skin hypersensitivity is a regular feature of allergic bronchopulmonary aspergillosis, not all positive reactors necessarily develop this disease (Khan et al. 1976). In earlier studies from this institute immediate hypersensitivity to *A. fumigatus* was reported by Sandhu et al. (1964) and Shivpuri & Agarwal (1969) in 3.6 % and 3.8 % of patients with chronic respiratory disorders, respectively. The late Arthus reaction, occurring 4–8 h after the Type I skin reaction, offers a better criterion for picking out suspected cases of allergic bronchopulmonary aspergillosis.

The finding of a 1.8 % overall prevalence of allergic bronchopulmonary aspergillosis in the study is not high enough to warrant any causal relationship between occupational exposure to *A. fumigatus* and aspergillosis. Furthermore, it may be noted that both the allergic bronchopulmonary aspergillosis patients belonged to group I of 30 workers with chronic respiratory diseases (Table 1), giving a prevalence of 6.7 % which is comparable to the prevalence observed (6.3 %) in a larger study from Delhi, covering 1007 patients with chest diseases (Khan 1976). The absence of precipitins in 98.2 % of the workers further suggests that perhaps actual colonization of the host rather than mere inhalation of fungal spores is required to raise the titre of precipitating antibodies to detectable and clinically significant levels. Our observations would therefore support the current epidemiologic concept that a constitutional predisposition of the host may be a more important factor than the extent of exposure to the fungus in the development of this disease.

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