

What does a fungus among us really mean?

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In this issue of the JOURNAL, two groups of investigators examine, by different means, the prevalence of a fascinating organism, *Aspergillus*. Schwartz and his colleagues¹ look at the incidence of sensitization in groups of Cleveland and London asthmatics, while Solomon and his co-workers² determine airborne levels of *Aspergillus* outside and within a midwestern university hospital and compare the indoor levels to that reported from England.

The genus of mold *Aspergillus* is a hardy organism that has been demonstrated in many diverse sources including soil, air, and decaying vegetation. It is one of the most commonly cultured molds from homes, being found in basements, crawl spaces, bedding, and house dust.

Several lung diseases in man can result from *Aspergillus*. These include invasive or septicemic aspergillosis, in which there is invasion of the bronchial wall producing a definite bronchitis; the saprophytic form or aspergilloma in which there is superficial invasion of a bronchiectatic cavity or bronchogenic cyst; bronchial asthma; hypersensitivity pneumonitis (extrinsic allergic alveolitis); and allergic bronchopulmonary aspergillosis. This last condition has captured the fancy of allergists and clinical immunologists. Diagnostic criteria include episodic asthma, pulmonary infiltrates, peripheral blood and sputum eosinophilia, immediate and sometimes late skin reactivity to *Aspergillus*, precipitating antibody to *Aspergillus*, markedly elevated serum IgE, and central bronchiectasis.

While no comparative studies have been reported

on the relative incidence of human disease due to *Aspergillus* in the United States and in England, there seems to be a greater incidence of allergic aspergillosis in Britain. It is the commonest form of asthma and pulmonary eosinophilia in the United Kingdom, comprising about 80%. While reports from Britain include series of as many as 111 patients,³ the two largest series in the United States are 30⁴ and 20⁵ patients, respectively. Hoehne, Reed, & Dickie⁶ felt in 1973 that this difference was more apparent than real. They believed many cases were missed because of false-negative skin tests and precipitin tests due to the low potency and variability of the antigens available from commercial sources in this country. In the last five years, however, a heightened index of diagnostic suspicion on the part of physicians and increased efforts to produce potent antigens in the United States are apparent.

A second reason for a difference in incidence might be regional variations in human exposure to the fungus. There are almost certainly geographic differences in the incidence of allergic bronchopulmonary aspergillosis. While the disease is frequently reported in urban dwellers, it is definitely more common in certain agricultural areas of Britain where exposure to high atmospheric spore concentrations may occur. Patients will also have frequent episodes of illness during the winter months in Britain where *Aspergillus* spores are found 100 times more commonly in the air from October to February.⁷ This report of Noble and Clayton⁷ is based on indoor recovery from hospital wards. Studies by Solomon and his colleagues performed in Ann Arbor, Michigan, have shown low-recovery *Aspergillus fumigatus* in homes⁸ as well as university libraries and animal care facilities.⁹ In this issue of the JOURNAL, this same group, utilizing comparable sampling sequences, found indoor levels of *A. fumigatus* in Ann Arbor to be substantially below those reported by Noble and Clayton and to lack any strong seasonal trend.² Outdoor levels sampled from an unobstructed hospital rooftop were also low. A report from Wales¹⁰ approximates that of Solomon,

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although a winter peak of prevalence was also evident. The data thus suggest substantially lower indoor exposure levels of *A. fumigatus* in midwest United States than those noted in London. As another corollary, Slavin and Winzenburger¹¹ reported the incidence of immediate skin reactivity to *Aspergillus* to be much less than to *Alternaria* in a group of outpatient atopics in their midwestern United States community.

Schwartz and co-workers,¹ in the current issue of this JOURNAL, attempt to survey the frequency of sensitivity to *Aspergillus* antigen on both sides of the Atlantic by determining immediate skin reactivity and serum precipitating antibody to *A. fumigatus* in reasonably comparable groups of asthmatics in Cleveland and in London. They cite previous studies which show differences in incidence of immediate skin reactivity. One possible reason for this variability was obviated in this study by using the same antigens for skin testing. Antigens for precipitin testing were different isolates of *A. fumigatus* strains but identically processed. These results indicate that frequency of sensitization was similar in Cleveland and London asthmatics, with 28% of Clevelanders and 23% of Londoners showing immediate skin reactivity and 7.5% of Clevelanders and 10.5% of Londoners demonstrating serum precipitating antibody to *A. fumigatus*. An interesting direct correlation between *Aspergillus* reactivity and airflow obstruction was demonstrated. An explanation for this might be that the tenacious mucus and marked bronchoconstriction typical of severe airflow obstruction potentiate the trapping of the short-chain *A. fumigatus* spores in the bronchial tree. In the larger subsegmental bronchi the spores grow exceedingly well at body temperatures, a temperature at which the growth of most molds is inhibited. It must be remembered that a cardinal feature of allergic aspergillosis which distinguishes this disease from other examples of allergy to inhaled antigens is that the antigen source can grow in the bronchial lumen and continually shed antigens into the tissues. The authors conclude that skin reactivity to *Aspergillus* is related to severity of airflow obstruction and atopic status and that the geographic location on either side of the Atlantic is not a determining factor.

What meaning these data have in terms of the relative frequency of serious disease from *Aspergillus* in the United States and in the United Kingdom remains to be seen. The presence of immediate skin reactivity

and precipitating antibody to *Aspergillus* is only an indication of antigenic exposure and an immunologic response to that exposure. Immediate and late skin test responses to *Aspergillus* have been reported in 4% of apparently normal individuals and in 36% of allergic asthmatics.⁵ Presence of precipitating antibody to *A. fumigatus* has been demonstrated in 9% of hospitalized patients, 3% of healthy office workers, and 12% of allergic asthmatics. It could well be that a mild exposure to the fungus such as seen in the midwestern United States suffices to sensitize the individual, while a heavy exposure as seen in London is necessary to develop the degree of colonization of the airway which results in the clinical disease allergic aspergillosis.

Schwartz's study¹ follows in the long tradition of Anglo-American cooperation and is a splendid example of the value of international collaboration in settling scientific questions. One can hope that this might well serve as a model for the study of other conditions in which geographic locale plays an important and determining role

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