

Alternaria-Associated Asthma

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In addition to house dust mites, there is increasing evidence that mold allergens, especially *Alternaria*, are implicated in contributing to allergic reaction, rhinitis, and asthma indoors. Situations leading to the exacerbation of asthma in an employee were investigated and subsequent medical evaluations were performed. An industrial hygiene study was conducted and bioaerosol testing revealed several mold allergens were present. However, based on the medical evaluation and testing results (skin prick test and radioallergen sorbent test [RAST]), it was concluded that *Alternaria* was inducing the respiratory reaction. *Alternaria* was present in the drip pan of the air conditioner unit and remedial actions were taken to remove the mold. Post-remedial bioaerosol sampling results revealed *Alternaria* was no longer present in the air and the employee returned to the office without recurrence of symptoms. Practically, several factors should be considered prior to concluding an association between exposure and illness. First, the employee's symptoms and signs should be consistent with a medical diagnosis. Second, there should be either in vitro or in vivo evidence of exposure. Third, environmental assessment should reveal evidence of plausible biological exposure. Fourth, there should be substantial improvement or even resolution of the illness after appropriate remediation of the health hazard. This case study illustrates the importance of teamwork by industrial hygienists and occupational health physicians in treatment and prevention of occupational and environmental diseases.

Keywords *Alternaria*, Asthma, Bioaerosol, Mold, Occupational Disease

Alternaria is a fungal species that belongs to fungi imperfecti or phylum Deuteromycota. This is a group of fungi characterized by the lack of an observed sexual phase in the life cycle. Imperfect fungi include species such as *Penicillium* which produces penicillin, and common outdoor molds such as *Alternaria* and *Cladosporium*.

Numerous fungal spores have been implicated in allergic reaction, rhinitis, and asthma. Over the last 20 years, the strength

of the relationship between specific antigens detected by IgE RAST or by skin prick test in asthma has become more precisely defined. Although the most frequent positive skin test or specific IgE antibody related to asthma is sensitivity to house dust mite (*Dermatophagoides*), more evidence has linked mold allergens to asthma, especially *Alternaria*.

CASE REPORT

A 33-year-old female police officer with a past history of allergy was evaluated for shortness of breath and chest tightness. The patient had been working as a police officer for the past 12 years. In the first 7 years, she performed duties as a patrol officer. After that she was involved in police recruitment for two years. Approximately 3 years ago, she started an assignment as a field training coordinator. She stated that she had been able to perform her duties both in the office and field setting with no previous health problems. Then, approximately 2 months ago, her office was relocated to a facility next to the police pistol range. Within a few days after she moved into this new office, she started experiencing a runny nose, constant coughing, and eventually wheezing and difficulty in breathing. She also indicated that upon leaving the office, her symptoms typically would become less intense but not completely subside. As a result of her increased symptomology, she consulted her personal physician who made a diagnosis of reactive airway disease and provided her with a Proventil (albuterol) inhaler and an antihistamine for allergy symptoms. She continued this treatment regimen for 1 1/2 months with no significant improvement. At that time, she suspected that her symptoms might be related to her relocation to the new office environment.

During the second office visit, her family doctor also suspected that there may be an occupational connection with her recent onset of asthma and relocation to her current office. She was referred to an occupational medicine physician for evaluation. Further medical history revealed that there was a positive family history for asthma. Her brother has asthma. She has always been a non-smoker. She admitted that she has a cat at home but does not appear to react to it. A review of her medical records indicated that she had been evaluated by an allergist 7 years ago for allergic rhinitis and exercise-induced bronchospasm controlled

with a pre-exercise bronchodilator inhaler. There had been no exacerbation of her respiratory symptoms until 2 months ago. Allergy testing by skin prick performed at that time showed positive reactions to several seasonal grasses, cat epithelia, dust mites, and *Alternaria*.

Upon physical examination, the patient appeared to be in no acute distress. Her respiratory rate was normal. There was no evidence of respiratory distress or use of accessory muscles. The eye, ear, nose, and throat examinations were normal. Chest examination showed normal breathing sounds without rhonchi. There was some expiratory wheezing in the left upper lung field. There was no evidence of peripheral cyanosis.

Pulmonary function test revealed reduced FEV1 at 72 percent predicted, FEF25-75 at 59 percent predicted, and FEV1/FVC ratio at 79 percent predicted. There was a good response to the inhaled bronchodilator. Post-bronchodilation spirometry revealed FEV1 at 101 percent, FEF25-75 at 83 percent, and FEV1/FVC ratio of 95 percent predicted. The pulmonary test findings were consistent with a mild to moderate pulmonary obstruction with small airways dysfunction. Additional laboratory studies which included a complete blood count and chemistry panel, were all normal. A radioallergosorbent test (RAST) was obtained. The result indicated that the patient is fact allergic to cat dander, dog epithelia, and *Alternaria alternata*.

In view of her history of allergy and a temporal relationship between the sudden onset of asthmatic symptoms with her relocation to the new office, she was advised not to return to her new office and was temporarily placed at another location.

INDUSTRIAL HYGIENE STUDY

An industrial hygiene study of air quality was conducted at the work environment. A Metrosonics AQ-501 Air Quality Monitor was used to determine if adequate air quality was being maintained indoors. Monitoring results, averaged over a 5-day period, for CO₂, temperature, and relative humidity, revealed levels of 627 parts per million, 74.6°F, and 58.7 percent, respectively. Although the site investigation did not reveal visible mold or indications of water intrusion, bioaerosol sampling was an appropriate course of action due to the patient's history of mold allergy.

Bioaerosol sampling was conducted with malt-extract agar plates using an Andersen Model 10-880 Single Stage Microbial Sampler. Indoor samples were collected from the patient's desk (about 6 feet from the air conditioning [A/C] unit) while the outdoor control samples were collected near the A/C unit's outside air intake. Indoor sample results, reported as colony forming units/cubic meter (CFU/m³), revealed elevated *Alternaria* species accompanied by lesser counts of *Penicillium*, *Monilia*, and *Ulocladium* species. The outdoor sample contained primarily *Cladosporium* and *Penicillium* species. In order to identify the indoor source of *Alternaria*, a thorough inspection of the A/C unit was performed. Standing water was discovered in the bottom of the A/C unit. This was due to the improper drainage of drip pan condensate out onto the ground. Sterile swab samples

TABLE I
Results of bioaerosol sampling before/after remediation of office occupied by patient

Before remediation		
Location	Fungal type	CFU/m ³
Inside office	Yeast	10
	<i>Ulocladium</i> sp.	20
	<i>Penicillium</i> sp.	40
	<i>Monilia</i> sp.	50
	<i>Alternaria</i> sp.	130
Outside fresh air intakes	Sterile mycelia	20
	<i>Cladosporium</i> sp.	150
	<i>Penicillium</i> sp.	210
After remediation		
Inside office	<i>Aspergillus niger</i>	30
	<i>Aspergillus</i> sp.	50
	<i>Penicillium</i> sp.	60
Outside fresh air intakes	<i>Aspergillus</i> sp.	90
	<i>Penicillium</i> sp.	60

of the interior drip pan area confirmed the presence of *Alternaria* in the standing water.

Recommendations for proper drainage of water from the A/C unit and proper disinfection of the interior drip pan area were implemented. Upon completion of the remedial actions, a second set of bioaerosol sampling was conducted. The second set of bioaerosol sampling results indicated that while *Aspergillus* and *Penicillium* were present in the indoor and outdoor samples, *Alternaria* had been effectively removed and the mold was no longer present in the indoor air. (see Table I for results).

FOLLOW-UP MEDICAL EVALUTION

The patient was re-evaluated medically on several occasions. Treatments with an inhaler and antihistamine were prescribed. Her symptoms essentially resolved within one week after working in a different office. Upon completion of the A/C unit remediation, the patient was allowed to return to her new office. She had no recurrence of symptoms after this.

DISCUSSION

Among the mold allergens, *Alternaria* has been adequately studied as a potent sensitizing agent. It has been implicated as one of the mold allergens to cause asthma. An early report by Hopkins⁽¹⁾ raised the possibility that *Alternaria* could cause asthma. Early experimental studies by Harris⁽²⁾ and Pennington⁽³⁾ also established an association between *Alternaria* and asthma. The spores of *Alternaria* are multi-celled. They appear in chains, head to toe, from which their name derives. Spores are usually multi-septate, both transversely and longitudinally. They vary in width and length according to the species, usually between 8 to

TABLE II
Comparison of health effects of fungal exposure^A

Fungus	Allergy	Mycosis	Irritation	Toxicosis
<i>Alternaria</i>	+	+/-	+	+/-
<i>Penicillium</i>	+	+/-	+	+
<i>Stachybotrys</i>	+	+/-	+	+
<i>Claviceps</i>	+	+/-	+	+
<i>Candida</i>	+	+	+	-
<i>Coccidioides</i>	+/-	+	+	-

^AModified from Fung et al. (1998).⁽⁸⁾

Legend: + reported, +/- possible, - not reported.

15 microns in size. Some *Alternaria* species have larger spores. There are animal models regarding *Alternaria*'s ability to induce sensitization.⁽⁴⁾ It has been demonstrated that *Alternaria* is a potent asthma allergen.^(5,6)

Scientific literature has provided only limited analysis of *Alternaria* allergens in indoor environments.⁽⁷⁾ Therefore, an estimation of a risk level for symptom exacerbation or determination of what is a high level of fungal spores at this time is premature. Although there may be a threshold concentration below which no symptoms are experienced, there are no data to conclude that such threshold can be derived at this time.

Recently, biological contaminants such as mold associated with water-damaged buildings have attracted the attention of health care professionals and the public. There are four mechanisms that a mold can cause human disease: allergy, mycosis, irritation, and mycotoxicosis. Table II outlines a comparison of selected fungi and their potential health effects.⁽⁸⁾

The ability of airborne mold particles to reach different parts of the respiratory tract depends upon the aerodynamic diameter of the particles. Large particles over 10 microns may not be capable of penetrating into deeper lung tissues. However, some mold spores are less than 10 microns in aerodynamic diameter⁽⁵⁾ and therefore are capable of penetrating into deeper lung tissues. As a result, an allergic reaction may ensue.

In addition to an allergic reaction, mold is capable of producing mycosis or infection. However, fungal infection typically occurs in a special situation where the patient is immunocompromised or under treatment with immunosuppressant medications. Fungus can also produce mycotoxins which are secondary metabolites. The most well known mycotoxins include aflatoxins produced by *Aspergillus flavus*, ergots produced by *Claviceps*, and trichothecenes produced by *Stachybotrys atra* and *Fusarium*. Molds can also produce a variety of organic chemicals including geosmins, alcohols, aldehydes, and sulfur-containing chemicals causing the typical earthy and musty odor.⁽⁹⁻¹²⁾

In the occupational setting there are several reports and studies implying various adverse health effects among occupants working in water-damaged buildings and/or offices. Biological contaminants have been implicated in those cases. Since water

TABLE III
Partial list of commonly encountered water sources found around the building^A

Outdoors	Indoors
Cooling towers	Humidifiers
Sprinkler/landscape drainage	Leaky appliances and plumbing
Air conditioning drainage	Leaky roofs
Sewer drains	Water-damaged carpets, walls
Wood piles	Bathroom showers, tubs
Compost piles	Condensation on windows, ducts, and insulation
Agricultural/Industrial storage	Improper construction designs

^AModified from Selzter (1994).⁽¹³⁾

is the essential ingredient for mold survival, potential water or moisture intrusion sources in or around buildings must be identified when symptoms of the occupants are consistent with biological contaminant exposure. If not properly maintained, the heating, ventilation, and air conditioning systems and cooling units such as water towers, evaporative coolers, drip pans, humidifiers, and vaporizers may accumulate stagnant water where mold and other biological agents can amplify. Table III provides a partial listing of potential water sources that can be found in or around a building.⁽¹³⁾

Several important lessons can be learned from this case report. First, the clinical symptoms and signs were consistent with the medical diagnosis.⁽¹⁴⁾ Second, the patient had a positive in vitro and in vivo test for a biological allergen (i.e., *Alternaria*).⁽¹⁵⁾ Third, an environmental and industrial hygiene study confirmed the presence of the specific biological allergen. Fourth, after identifying the source of the biological contaminant, remedial action was performed. Fifth, the patient responded to proper medical treatment and avoidance of allergens. Upon returning to the environment which was properly remediated, the patient had no additional symptoms or disease recur.

In summary, biological contamination is a commonly encountered occupational and environmental as well as public health issue. Occupational health professionals should be cognizant of recognizing symptoms consistent with a biological exposure. Future research in biological contamination and adverse health affects may include the following areas: assessment of water-contaminated buildings using the American Conference of Governmental Industrial Hygienists (ACGIH®) bioaerosol assessment and control guidelines;⁽¹⁶⁾ and documentation of human exposures to known mold allergens and their byproducts that result in clinical syndromes compatible with diagnosable diseases. Furthermore, periodic and preventive maintenance of building components to avoid water intrusion may be

as important as early recognition and treatment of health effects secondary to biological contamination.

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