MYCOLOGY ANSWERS

TO WHAT EXTENT DO AIRBORNE FUNGAL SPORES CONTRIBUTE TO RESPIRATORY DISEASE AND ALLERGIC REACTIONS IN HUMANS?

It is quite clear to anyone who has left laboratory culture media exposed to the atmosphere, even very briefly, that fungal spores are all around us and therefore, that we must be breathing them in and out during our normal daily routines. For example, clearing leaves and windfalls in Autumn, it is often easy to see clouds of spores dislodged from the surfaces of rotting plant material. For the most part, these spores have little or no effect on us and we need not consider them further. However, inhaled fungal spores can cause a number of conditions in humans with various consequences. Allergic responses, usually reactions to the proteins in the spore wall, can result in the development of a runny nose and eyes (allergic rhinitis), and asthma-like symptoms which are especially distressing in individuals who develop exaggerated allergic responses (hypersensitive or atopic individuals). Prolonged exposure to unusually large numbers of spores, often as the result of occupational circumstances, can result in the development of allergic alveolitis. In addition, some fungal species are primary pathogens, invading the body through the respiratory tract, and others can act a secondary pathogens, invading in circumstances where the host is predisposed to infection.

There is a range of particles that occur in outdoor atmospheres which may give rise to allergic responses in humans, e.g. dust, fibres and grit, pollen grains from higher plants (particularly grasses and trees) and also spores (both dry and slimy spores) of fungi and filamentous bacteria (Actinomycetes). The most abundant spores associated with allergenicity to occur in air arise from fungi commonly found on leaf surfaces, for example *Cladosporium* Link, *Sporobolomyces* Kluyver & v. Niel, which grows as yeast-like cells and forms large numbers of spores (ballistospores), *Didymella* Sacc:Sacc and *Alternaria* Nees. Such spores may act as allergens although no tissue invasion occurs.

Dry-spored fungi are often implicated in allergic responses. However, it is not altogether clear whether it is the numbers of the particles involved or the volumes that are more important in inducing allergic responses in humans. It is interesting that while the numbers of fungal spores recorded in air samples may be high the spores themselves are extremely tiny. Although there may be larger numbers of fungal spores in a given volume of air than pollen grains, the volume concentrations of those pollen grains may actually be larger. Fungal spores are often only a few microns in diameter and the majority of spores that occur in breathable air are less than 100 μm diameter. An average pollen grain occupies the same volume as 200 *Cladosporium* spores. Additionally, it is often the case that those fungal spores produced in huge numbers are smaller in size. Large fungal spores such as those of *Alternaria* spp. may become deposited in the nose whereas smaller spores e.g. those of *Aspergillus* species (3-5 μm diameter) may pass further down into the respiratory tract because of their size. Sedimentation rates depend on a range of factors including spore size, shape, wettability and the architecture of the spore wall.

Rainfall has a large effect on the occurrence of spores in the air. Washout of larger spores occurs rapidly but small particles will remain airborne for longer although these too are picked up by rain drops. It has also been noted however, that acute asthma attacks may occur immediately following rain storms or within a few hours of heavy rainfall. It is likely that this effect can be attributed to a sudden increase in water availability encouraging the release of spores from fungal fruiting structures. The after-effect of a storm actually increases the number of new spores reaching the atmosphere. In addition, seasons and location have a marked effect on numbers of spores in the atmosphere and to some extent the range of types of spore present. There can be marked fluctuations in numbers due to differing local circumstances, such as the occurrence of fungal crop disease and the concomitant increase in release of spores from diseased plants.

Indoors, airborne spores may represent a different mix of species. In the home environment there

are usually less spores than outdoors and fewer species will be represented. In office buildings, the type of ventilation system and the amount of air disturbance will influence the species range and numbers of spores present. Air conditioning systems can markedly influence the distribution of spores and humidifiers may encourage sporulation of particular species (often actinomycetes), representing an additional source of contamination. The representative microflora of an indoor occupational environment will be related to the work being carried out and to the actual conditions. Damp grain and hay are particularly hazardous sources of spores (*A. fumigatus* and *A. versicolor*) during storage and at harvest. Moulded hay will give rise to large spore clouds when disturbed and has been reported to contain 10^9 propagules per gram of hay. Materials stored for use in food manufacture (particularly grains, flours, nuts, meals, ripening cheeses and raw materials such as fruits) may also harbour fungal spores. Mushroom farms, saw mills, paper mills, composting areas, waste disposal sites and processing plants where fungal contamination may occur, are all areas where potentially greater numbers of allergenic particles may be present. Allergic conditions can arise as the result of prolonged and/or repeated exposure to unusually high concentrations of spores, sometimes representing a particular occupational hazard. For example, Malt worker's lung, caused by *Aspergillus clavatus*, *A. fumigatus* and *A. flavus* (allergic aspergillosis), Farmer's lung caused by spores from the actinomycetes *Micropolyspora faeni* and *Thermoactinomyces vulgaris* and Cheese washer's lung, caused by *Penicillium casei* spores. In addition, exposure to some fungal metabolites, particularly enzymes (proteases, amylase, cellulase) can also result in the development of allergic responses, affecting those in occupations such as baking and the fermentation industries. Toxins (mycotoxins) produced by some fungal species have also been implicated in the development of respiratory problems although there is little information to support this theory.

Some fungi can act as secondary pathogens on humans. This can result from the growth of species which would normally colonise dead and decaying material (saprophytic fungi) taking the opportunity to grow as pathogens. *Aspergillus fumigatus* occurs commonly on dead organic material in compost heaps and in stored grains and hay where it can withstand the higher temperatures reached by the decomposing plant material. It is therefore also able to grow at body temperature. *A. fumigatus* causes allergic reactions but does not invade healthy tissues. It can however, act as a secondary pathogen, affecting patients where lung tissues have been previously diseased. Spaces within damaged lung tissue and plugs of excess mucus may be colonised, causing severe allergic reactions and forming a ball of mycelium (aspergilloma) eventually resulting in severe breathing difficulties. More deeply seated infections can develop in very ill and highly susceptible patients where *A. fumigatus* becomes invasive. This only occurs when immunological defenses are severely disrupted such as in transplant patients.

Primary infections by fungi can also occur via the respiratory tract. Some fungi, often found in warm regions of the world, are invasive pathogens. *Coccidioides immitis* causes 'Valley fever' in dry regions of Southern USA and Mexico; *Histoplasma capsulatum* causes Histoplasmosis in Central USA; *Blastomyces dermatitidis* causes Blastomycosis in Eastern USA and Canada and *Paracoccidioides brasiliensis* causes Paracoccidioidomycoses in Central/South America. These species form spores in soils, plant debris and bird droppings disturbance of which causes spores to become airborne. Inhalation of spores can give rise to lung infections which in many cases may heal spontaneously, especially in healthy individuals, and pass undetected. Indeed it is probable that huge numbers of people are affected without note. However, in more susceptible patients the infections may spread through the blood stream (rapidly becoming systemic) and may eventually cause extensive tissue destruction. Where susceptibility to infection is high and resistance low this may have fatal consequences.

Most people will never encounter any systemic mycoses and, with care, most allergic reactions can also be avoided or minimised. Nevertheless, it is important that the effects of exposure and sensitization are taken seriously and monitored, so that control measures may be implemented if necessary.

Susan Isaac
Department of Genetics & Microbiology,
Life Sciences Building, University of Liverpool,
Crown Street, Liverpool, L69 3BX