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REVIEW PAPER

Allergenicity of airborne basidiospores and ascospores: need for further studies

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Abstract Many known fungal species are grouped among basidiomycetes and ascomycetes. Active mechanisms of spore release into air currents are among the main features of these fungi. Aerobiological studies have described their presence in many regions worldwide. In some areas, fungi have been described as the predominant outdoor airborne biological particulate with much higher concentrations than pollen. Other studies have determined that among the fungal aerospora, the highest concentrations belong to basidiospores and ascospores. Nevertheless, the allergenic potential of spores from basidiomycetes and meiotic forms of ascomycetes has not been studied to the extent of mitosporic fungi and allergens from other sources. The need to further evaluate the role of basidiomycetes and meiotic ascomycetes in allergies is evidenced by the few genera with characterized allergens and limited studies that had demonstrated levels of sensitization similar or higher to that of mitosporic fungi and other allergens. In this review, based on the existing aerobiological, epidemiological, immunological, and molecular biology studies, we provide evidence that the role of basidiomycetes and ascomycetes deserves more attention with respect to their roles as potential aeroallergens.

Keywords Allergen · Airborne · Basidiomycete · Ascomycetes · Basidiospore · Ascospore

Abbreviations

AR	Allergic rhinitis
Asco	Ascospores
AS	Asthma
Basid	Basidiospores
Deutero	Deuteromycetes/mitosporic fungi
H/F	Hyphae and fragments
IgE	Immunoglobulin E
NAR	Nonallergic rhinitis
unID	Particles not able to be identified
WHO/IUIS	World Health Organization and International Union of Immunological Societies Allergen Nomenclature Sub-committee

1 Introduction

The fungal kingdom is composed of members usually known for their ability to degrade organic nonliving or

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dead material (Alexopoulos et al. 1996; Stephenson 2010). The vast majority share features with plants, such as being eukaryotic, having cell wall, absorptive nutrition, and some reproduce sexually and others asexually. Contrary to plants, they do not produce sugars through photosynthesis and their dispersal structures (spores or conidia) and absorptive filaments (hyphae or mycelia) are much smaller than those of plants (Alexopoulos et al. 1996; Stephenson 2010). In addition, many fungi have structural components found in the exoskeleton of insects and arthropods, such as chitin (polymer of *N-acetylglucosamine*) and β-glucans (polymer of glucose), which are important structural components fungal cell walls (Stephenson 2010). With respect to diseases, fungi also share one important feature with animals and plants: the potential to induce allergies.

Basidiomycetes (phylum Basidiomycota) and ascomycetes (phylum Ascomycota) are two important groups within the fungi kingdom. They are widespread in different environments throughout the world, and a variety of species can be present depending on the characteristic climate of a particular region or season (Horn et al. 1993; Alexopoulos et al. 1996; Stamets 2002). They play different and important roles in many ecosystems, such as degrading organic matter and facilitating the absorption of nutrients, and some are often found parasitizing other organisms (Alexopoulos et al. 1996). In addition, there are species that are commercially distributed (e.g., gilled mushroom *Pleurotus ostreatus*), many are poisonous (e.g., gilled mushrooms *Chlorophyllum molybdites* and *Amanita muscaria*, etc.), and others are rarely noticeable in their ecosystems (Horn et al. 1993; Alexopoulos et al. 1996; Stamets 2002).

The structures responsible for the dispersal of fungi (spores) are present in the atmosphere of many areas. Numerous studies have described their presence in air, but most of these investigations have been performed in temperate regions (Table 1) (D'Amato and Spieksma 1995; Horn et al. 1995; Burge and Rogers 2000; Troutt and Levetin 2001; Burch and Levetin 2002; Burge 2002; Levetin and Horner 2002; Agashe and Caulton 2009; Quintero et al. 2010). Basidiospores and ascospores are among the predominant airborne biological particles in these studies. For these reasons and the small size of many ascospores and basidiospores that allows them to reach deep into the respiratory tract (Horn et al. 1995; Levetin and Horner 2002; Horn et al. 2004), their potential to cause exacerbations of respiratory diseases should not be disregarded.

Table 1 Aerobiological studies in which basidiospores and ascospores were found to be predominant in the atmosphere

Author (year published)	Location
Jenkins et al. (1980)	UK
Levetin (1990)	USA (Midwest)
Comtois and Mandrioli (1996)	Middle East (Adriatic Sea)
Delfino et al. (1997)	USA (West)
Sterling et al. (1999)	USA (Midwest)
Agashe and Vidya (1999)	India
Craig and Levetin (2000)	USA (Midwest)
Dales et al. (2000)	Canada
Troutt and Levetin (2001)	USA (Midwest)
Chakraborty et al. (2001)	India
Mitakakis et al. (2001)	Australia
Hasnain et al. (2005)	Saudi Arabia
Morales et al. (2006)	Spain
Green et al. (2006a, b, c)	Australia
De Antoni Zoppas et al. (2006)	Brazil
Bianchi and Olabuenaga (2006)	Argentina
Herrero et al. (2006)	Spain
Pyrri and Kapsanaki-Gotsi (2007)	Greece
Grinn-Gofroń and Mika (2008)	Poland
Khattab and Levetin (2008)	USA (Midwest)
Quintero et al. (2010)	Puerto Rico

The allergenicity of fungi has been recognized, but their allergens have not been studied as those from other sources such as animal, plants, food, among others. Although there are studies that have described the presence of sensitivity to basidiomycetes and ascomycetes among subjects with respiratory allergies (Sprenger et al. 1988; Horner et al. 1992; Lehre et al. 1994; Helbling et al. 2002), there is limited literature about their allergens compared to that of mitosporic fungi (spores produced asexually), such as *Alternaria* spp., *Penicillium* spp., and *Aspergillus* spp. It is surprising that basidiomycetes and ascomycetes have not been more widely investigated given their potential allergenecity, and that their widespread distribution and ability to release numerous spores makes them a potential important contributor to the biological component of particulate matter (Hyde 1972).

The purpose of this review is to describe the importance of basidiospores and ascospores as allergens based on the current aerobiological, epidemiological, and immunological studies that have been performed in different regions worldwide. In addition, evidence will be provided to support the need for more studies to better define the role of basidiomycetes and ascomycetes in allergic respiratory diseases.

2 Mycology of basidiomycetes and ascomycetes

The phylum Basidiomycota is composed of a large and diverse group (approximately 30,000 species) of fungi that includes puffballs, mushrooms, boletes, earthstars, stinkhorns, bird's nest, jelly fungi, bracket, rusts, and smuts (Fig. 1) (Ingold and Hudson 1993; Alexopoulos et al. 1996). They can be found in a wide range of substrates (e.g., on trees and forest litter, grass lands, and wood products) degrading cellulose and lignin, processes important for the organic cycle. Others are parasites of various crops (e.g., smuts and ruts) or contribute to the life cycle of higher plants (Horn et al. 1993; Alexopoulos et al. 1996; Morales 2006). In addition, many have been used for centuries for natural medicine purposes in many regions, such as in East Asian societies (Stamets 2002).

In contrast with mitosporic fungi (Fungi Imperfecti and formerly known as deuteromycetes) which produce spores by mitotic division, basidiomycetes are meiosporic (spores result from meiosis) fungi that produce haploid sexual spores, or basidiospores, usually in groups of four on a specialized structure known as a basidium (basidia in plural; Fig. 2a) (Alexopoulos et al. 1996; Morales et al. 2006). Furthermore, while mitospores (spores from mitotic

Fig. 1 Examples of some basidiomycetes. **a** Gilled mushroom (*Mycena spp*); **b** jelly fungi (*Auricularia auricular*); **c** polypore (*Ganoderma applanatum*); **d** earthstar (*Geastrum triplex*); **e** boletes (*Boletus roseopurpureus*); **f** puffball (*Morganella fuliginea*); **g** stinkhorn (*Dictyophora indusiata*). Notice the spore deposits on the leaves under the fruiting body of *G. applanatum*, which releases trillions of spores daily. Images D through G are courtesy of Dr. Deborah J. Lodge

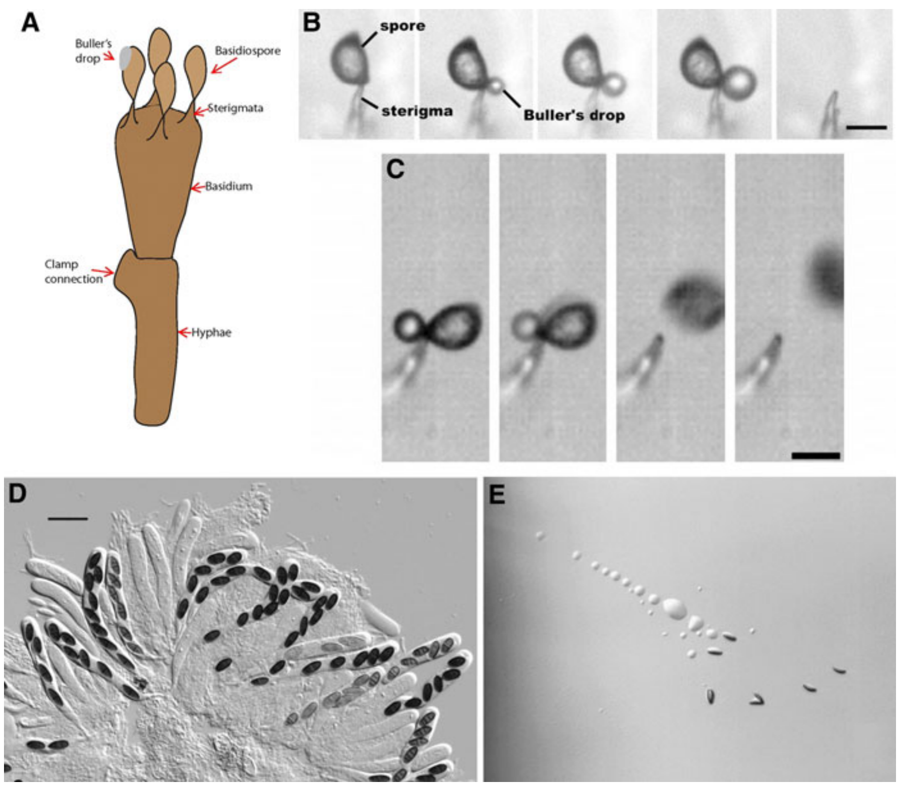

Fig. 2 Mechanisms of spore release for basidiospores and ascospores. Humidity nearby the canopy of the fruiting body leads to the accumulation of water on the basidiospore-bearing structures in basidiomycetes (**a**). As the water droplet, or Buller's drop, begins to grow the gravitational center of the spore is shifted. Once the Buller's drop reaches the end of the spore where it is attached to the sterigmata, the sudden movement of the spores caused by the Buller's drop leads to its release from its point of attachment (**b**, **C**). With ascomycetes, in normal conditions there are usually 8 ascospores inside the ascus (**d**). Once humidity increases in the environment where the ascomycetes are found, an increase in osmotic pressure (dashed red arrows) begins to accumulate inside the ascus. The osmotic pressure keeps rising and cluttering the ascospores at the top of the ascus until they are eventually ejected (**e**). **b**, **c** correspond to reference Pringle et al. 2005; **d** from Phillips et al. 2005; **e** from Trail et al. 2002. Reprinted with permission from *Mycologia* © The Mycologial Society of America

fungi) are released by a passive mechanism or external force (e.g., nearby wind currents) for dispersal from their spore-bearing structures, basidiospores are released by an active mechanisms associated with humidity and the Buller's drop that affects the gravitational center of the spore causing it to be catapulted and released (Fig. 2b, c) (Pringle et al. 2005). This is one of the reasons why after a rain event, when relative humidity increases, high concentrations of basidiospores in the atmosphere are often recorded (Fig. 3) (Levetin 1990; Isard and Gage 2001; Quintero et al. 2010).

Members of the phylum Ascomycota, constituted with nearly 25,000 members, share many characteristics with that of basidiomycetes with respect to habitats, functions in nature, meiotic division for spore production, and an active mechanisms for the release of the spores (Kendrick 1992; Ingold and Hudson 1993; Alexopoulos et al. 1996; Blackwell et al. 2006). As the name implies, the sexual spores (ascospores) of this group are in an ascus (asci in plural; Fig. 2d,e) usually in groups of eight and released when the osmotic pressure inside the ascus increases although other physical elements, depending on the genera, are also involved (Stensvand et al. 1997; Trail et al. 2002; Clarkson et al. 2003; van Heerden et al. 2005). It is important to clarify that within this phylum mitosporic fungi are classified (e.g., *Cladosporium*, *Fusarium*, *Alternaria*, etc.), but their spores, as mentioned before, are a result of mitosis. Mitosporic fungi are the asexual

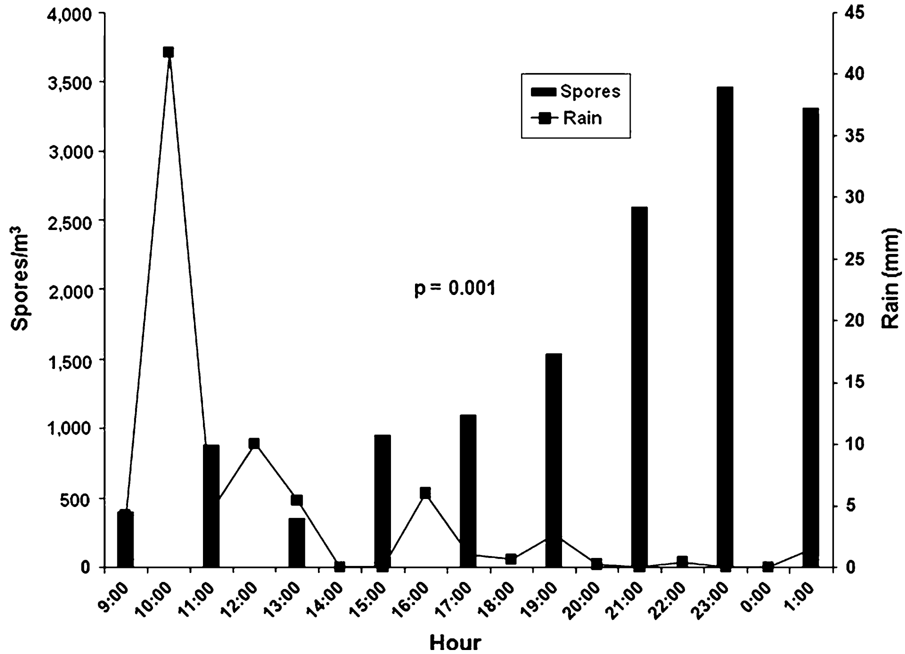

Fig. 3 Relationship between precipitation and total concentrations of spores in the atmosphere. Quintero et al. (6). Reprinted with permission from the publisher Springerlink

stage of ascomycetes (Blackwell et al. 2006) and are no longer grouped as a single group; however, they will not be discussed because the focus of this review are the sexual (meiotic) forms of ascomycetes.

3 Aerobiology of basidiospores and ascospores

Although the term aerobiology has had different definitions, it mainly involves the study of the particles of biological origin present in the atmosphere and the factors that directly or indirectly affect their source, liberation, transport, dispersal, deposition, and impact (Isard and Gage 2001; Burge 2002; Agashe and Caulton 2009). As a result, there have been numerous studies, at different locations around the globe, to determine the predominant outdoor airborne biological particles.

Fungal spores are a component of the atmosphere and in many studies in temperate and a few tropical environments they have been found to be the most predominant biological particulate (Gregory 1961; Kendrick 1992; D'Amato and Spieksma 1995; Horner et al. 1995; Burge 2002; Okten et al. 2005; Agashe and Caulton 2009; Quintero et al. 2010). Their patterns of prevalence are governed by multiple factors, including plants floristic patterns, agricultural practices, meteorological variables, amount of organic litter, and presence and age of colony and/or fruiting body, among others (Kendrick 1992; Alexopoulos et al. 1996; Horner et al. 1998; Burge and Rogers 2000; Magyar 2002; Ceter and Pinar 2009; Quintero et al. 2010). For example, in temperate regions, such as in the United States and Europe, spores appear in late winter becoming more prevalent in summer and fall. In the tropics, they seem to be prevalent throughout the year with the rainy season (Spring and Fall) showing the highest concentrations (D'Amato and Spieksma 1995; Bush and Portnoy 2001; Burton and Katelaris 2010; Quintero et al. 2010). There are also differences in the predominant fungi, with mitosporic fungi (e.g., *Alternaria sp.*, *Cladosporium sp.*, *Aspergillus/Penicillium*) being more prevalent in temperate regions, but basidiospores and ascospores predominating in tropical areas (Hasnain et al. 2005; Ceter and Pinar 2009; Burton and Katelaris 2010; Quintero et al. 2010).

3.1 Aerodynamic and atmospheric factors

Various combinations of atmospheric factors and innate characteristics of fungal species have different effects on the trajectory of air fungal spora. Wind speed and direction, temperature, humidity, rain, among others atmospheric variables have been extensively studied in different parts of the world and in different settings (i.e., urban and rural areas) with respect to their effects on concentration and dispersal of bioaerosols, including fungal spores (Hurtado et al. 1989; Nagarajan and Singh 1990; Madelin and Johnson 1992; Tan et al. 1992; Spieksma 1993; D'Amato and Spieksma 1995; Lewisn et al. 2000; Chakraborty et al. 2001; Levetin and Van de Water 2001; Troutt and Levetin 2001; Burch and Levetin 2002; Magyar 2002; Sakiyan and Inceoglu 2003; Horner et al. 2004; Newhouse and Levetin 2004; Rodriguez-Rajo et al. 2004; Burton and Katelaris 2010; Quinteroi et al. 2010). These investigations have also described the different mechanisms of spore liberation, concentrations of spores released per day, and the environmental conditions that influence the liberation and dispersal of spores from different fungi. Taken together, these studies have contributed important aerobiological information about spores, but there is a consensus that more studies are needed (Horner et al. 2004; Newhouse and Levetin 2004; et al. Morales et al. 2006; Agashe and Caulton 2009; Ceter and Pinar 2009; Quintero et al. 2010).

Among all atmospheric variables studied, wind is the most important for the dispersal of spores (Alexopoulos et al. 1996). Mitosporic fungi are fully dependent on the wind because their mechanism of spore release is passive and the air current moving nearby the spore-bearing structures is the force that liberates them (Alexopoulos et al. 1996). On the other hand, as mentioned previously, basidiomycetes and ascomycetes liberate their spores by mechanisms governed by the action of water (i.e., humidity and dew point) on the basidium or ascus. The phototropic and geotropic properties of these fungi contribute to their orientation toward the light and away from the grown, respectively. For agarics (spore-bearing structures within gills; Fig. 1a) and polypores (spore-bearing structures within pores; Fig. 1b), this allows the downward exit of the spores from the fruiting bodies, while other fungi such as those of puffballs (spore-bearing structures inside a ball-shape fruiting body; Fig. 1f) need to be oriented toward the light in order to release their spores once a rain drop impacts their surface. In this manner, the spores are easily accessible to turbulent currents flowing nearby the fruiting body (Isard and Gage 2001). Once airborne, other large-scale air movements, such as convection currents, low-level jets, global wind belts, and tropical and extratropical cyclones and anticyclones, can transport spores in patches, within and between landscapes, eco-regions, or between continents, respectively (Nagarajan and Singh 1990; Levizzani et al. 1998; Isard and Gage 2001).

The temperature of the air also plays a role in the movement of air spora but, contrary to air currents, its effect is mainly at ground level (i.e., enclosed place, within vegetation). When the temperature of the surrounding air or ground increases, a convection current moves the suspended particulate upwards; the opposite occurs when the air cools down, together creating a vertical dispersion gradient (Agashe and Caulton 2009). These events take place mainly in forests or where there are numerous fruiting bodies, but once they encounter turbulent air currents, the convection currents no longer contribute to transport within the atmosphere.

Water can also contribute to the concentration of spores in the atmosphere. Rain events of high intensity could clean the atmosphere by forcing down suspended spores, while small amount of rain can work at the leaf or fruiting body level by provoking the movement of fungal spores from the leaf surface with splashes or inducing the ejection of spores, respectively (Burge and Rogers 2000; Chakraborty et al. 2001; Levetin and Horner 2002). This mechanism is seen with dry spores that are often found parasitizing leaves, such as many of the mitosporic fungi (e.g., *Cladosporium spp*, *Alternaria spp*., etc.). As previously described, water that accumulates on the surface of fruiting bodies induces the liberation of spores from basidiomycetes by the action of the Buller's drop (Fig. 2b, c) on the gravitational center of the basidiospores or the increase in osmotic pressure inside the ascus forcing the ejection of spores in ascomycetes (Fig. 2e).

Basidiomycetes and ascomycetes are known to liberate numerous spores daily. This is one of the most important characteristics of these fungi and one of the reasons why, in few studies, they have been correlated with cases of chronic respiratory diseases, such as asthma and rhinitis (Bush and Portnoy 2001; Levetin and Van de Water 2001; Newhouse and Levetin 2004; Semik-Orzech et al. 2008). Plant pathogens, such as members of the genus *Ganoderma spp.* and *Puccinia spp.*, are known to produce trillions and millions of spores per square meter, respectively (Agashe and Caulton 2009). Similarly, other studies have found ascospores in high concentrations throughout the year in different areas of the world (Stensvand et al. 1997; Magyar 2002; Ceter and Pinar 2009; Quintero et al. 2010). Being widespread and the ability to liberate large concentrations of spores daily are two important aeroallergen characteristics (Hyde 1972; Gregory 1973) common to many basidiomycetes and meiotic ascomycetes.

4 Basidiospores and ascospores as allergens

4.1 Respiratory allergies

Respiratory allergies, allergic rhinitis, and asthma have been increasing worldwide (Braman 2006), and numerous studies have described the importance of airborne biogenic particulate matter in episodes of these diseases, including those of fungal origin (Hiddlestone 1961; Lewis et al. 2000; Green et al. 2003; Mari et al. 2003; Newhouse and Levetin 2004; Cho et al. 2005; Green et al. 2005a, b, c, 2006a, b, c; Semik-Orzech et al. 2008; Agashe and Caulton 2009). In addition, some investigations have found correlation between high concentrations of specific types of spores with morbidity and mortality from asthma (Packe and Ayres 1985; Targonski et al. 1995; Delfino et al. 1997; Black et al. 2000; Chew et al. 2000; Lewis et al. 2000; Newhouse and Levetin 2004). Although mitosporic fungi and pollen seem to predominate in temperate regions, some aerobiological and epidemiological studies performed in these areas have correlated asthma symptoms with concentrations of basidiospores (Jenkins et al. 1980; Delfino et al. 1996, 1997; Epton et al. 1997; Dales et al. 2000; Newhouse and Levetin 2004). In addition, some of these studies have also found association of respiratory allergies with meteorological conditions that are suitable for the release of basidiospores, such as high humidity and dew point (Morrow-Brown and Jackson 1985; Davidson et al. 1996; Lewis et al. 2000; Levetin and Van de Water 2001; Taylor and Jonsson 2004; Nasser and Pulimood 2009).

There have been various reports that have correlated high concentrations of ascospores in various areas with respiratory conditions (Jenkins et al. 1980; Troutt and Levetin 2001; Magyar 2002; Ceter and Pinar 2009). However, most of the epidemiological studies mentioned above have been performed in temperate regions despite basidiospores and ascospores being important component of the air spora in tropical areas. For this reason, the role of these fungal spores needs to be further studied emphasizing the tropics and their roles in cases of respiratory allergic diseases.

4.2 Allergens

Although the previous reports discussed mention basidiospores and ascospores being important components of the air spora, the vast majority of studies of fungal allergens have been performed in temperate areas where the testing for sensitization mainly relies on extracts from pollen and mitosporic fungi (Horner et al. 1995; Delfino et al. 1997; Chew et al. 2000; Green et al. 2003, 2005a, 2006a, b, 2009; Mari et al. 2003; Denning et al. 2006; Semik-Orzech et al. 2008; Agashe and Caulton 2009). Extracts from these agents are commonly included in the panels for skin-prick tests and immunological assays for detecting allergies. According to the database of World Health Organization and International Union of Immunological Societies Allergen Nomenclature Sub-committee (WHO/IUIS http://www.allergen.org/index.php) (Table 2), the majority of allergenic proteins fully described from fungi correspond to mitosporic species such as

Table 2 Comparison of total characterized allergens in animals, plants, and fungi

Allergen source	Characterized allergens
Animal	269
Plants	322
Fungi (Ascomycota)	79
Capnodiales (e.g., *Cladosporium spp.*)	10
Eurotiales (e.g., *Aspergillus/Penicillium* spp.)	45
Hypocreales (e.g., *Fusarium spp.*)	2
Onygenales (e.g., *Trichophyton spp.*)	4
Pleosporales (e.g., *Alternaria spp.*)	15
Saccharomycetales (e.g., *Candida spp.*)	3
Fungi (Basidiomycota)	22
Agaricales (e.g., gilled musrooms)	7
Malasseziales (e.g., *Malassezia spp.*)	13
Sporidiobolales (e.g., *Rhodotorula spp.*)	2

Source World Health Organization Allergen and International Union of Immunological Societies Allergen Nomenclature Sub-committee: http://www.allergen.org

Aspergillus spp, *Penicillium spp*, *Fusarium spp*, *Alternaria spp*, among others.

Despite the lack of commercial extracts for basidiomycetes, there have been studies in which the presence for sensitization to basidiomycetes has been investigated in subjects with respiratory allergies (Table 3). Shichijo et al. (1970) tested for allergies with *Cortinellus spp*. A study by Santilli et al. (1985) with dialyzed extracts demonstrated reactivity in subjects with asthma or allergic rhinitis to *Agaricus campestris*, *Coprinus micaceus*, *Fuligo septica*, *Lycoperdon perlatum*, *Scleroderma lycoperdoides*, and *Ustilago maydi*. In studies performed by Lehrer et al. (1986, 1994), between 25 and 30% of the participants reacted to at least one basidiomycete extract. Helbling et al. (1993a, b, 1998, 1999) found skin-prick test reactivity, allergen-specific (immunoglobulin E) IgE, and responses in nasal challenges in subjects with respiratory allergies with spore or mycelial extracts from *Psilocybe spp*., *Boletus spp*, *Coprinus spp*, and *Pleurotus spp*. Horner et al. (1988, 1989a, b, 1991, 1993a, b; 1995) has also worked extensively with basidiospore and mycelial extracts, and even identified a protein from the mycelium of *Psilocybe cubensis* (Psi c 2, a cyclophilin) as one of the allergenic components. Other investigations have tested sensitization to other basidiomycetes, studied the most appropriate elution mechanisms from spores, mycelia, or other fruiting body's tissues, demonstrated allergen-specific IgE reactivity, protease activity, and bronchial response, with the extracts, and molecular biology have been able to characterize few allergenic proteins (Lopez et al. 1985; Butcher et al. 1987; Liengswangwong et al. 1987; Ibanez et al. 1988; Sprenger et al. 1988; Lopez et al. 1989; Wongtim et al. 1993; Torricelli et al. 1997; Helbling et al. 1998; Brander et al. 1999a, b).

Other studies have investigated exposures to both basidiomycetes and mitosporic fungi, either for presence of similar antigenic and allergenic determinants or different reactivities. O'Neil et al. (1988, 1990) examined various extracts from both groups and suggested that similar epitopes may be present within basidiomycetes. O'Neil et al. (O'Neil et al. 1990) also suggested that there are significant differences in reactivity between basidiomycetes and mitosporic fungi. A study performed in the Pacific Northwest of the United States found that prevalence of basidiomycete sensitization in that area was similar to that of mitosporic fungi (Sprenger et al. 1988). Recently, in studies performed in San Juan, Puerto Rico (located in the tropical environment of the Caribbean) with subjects suffering from respiratory allergies mitosporic fungi demonstrated lower reactivities to that of basidiospores and ascospores, and even lower than airborne fungal fragments (Figs. 4 and 5) (Rivera-Mariani et al. 2011a, b). These studies demonstrate the importance of testing for different fungal allergens not commonly included in panels to detect allergies and with methodologies that are not extract-dependent because it is known that with conventional techniques to detection sensitization assume that the causative agent is included in the panel of extracts being tested.

5 Need for further studies

The reports previously discussed clearly demonstrate the importance of spores from basidiomycetes and meiotic forms ascomycetes, either through their spores, mycelia, or other source as potential allergens. The knowledge of specific allergenic proteins from these groups of fungi is still limited and is far less than our understanding of many other sources of allergen. One reason for this discrepancy is that extracts from some mitosporic fungi are commercially available and less difficult to obtain in laboratory conditions. Basidiomycetes and ascomycetes are very difficult to cultivate in laboratory settings and to obtain material for extracts. In addition, many of these can be identified in air samples but their fruiting bodies are rarely or difficult to locate in forest areas. It seems that one strategy that could be used would be to test them directly from air samples, and the development of an immunoblotting technique known as the halogen immunoassay has allowed testing airborne fungal spores for reactivity in subjects with respiratory allergies by challenging their sera directly with air samples (O'Meara et al. 1998; Mitakakis et al. 2001; Green et al. 2003, 2005a, b, c; 2006, 2009; Rivera-Mariani et al. 2011b).

As discussed in previous sections, spores from basidiomycetes and meiotic forms ascomycetes are common in the environment, and in some places are in higher concentrations than that of mitosporic fungi in some places. Recently, through molecular biology basidiomycetes were detected in indoor and occupational settings (Rittenour et al. 2011). Given the

Table 3 Studies in which sensitization to basidiomycetes was investigated

Author (year)	Place	Basidiomycetes tested
Schihijo et al. (1970)	Japan	*Cortinellus shiitake*
Santilli et al. (1985)	USA (Eastern)	*Agaricus campestris,*
		Coprinus micaceus
		Fuligo septica
		Lycoperdon perlatum
		Scleroderma lycoperdoides
		Ustilago maydi
Lopez et al. (1985, 1989)	USA (Southeast)	*Cantharellus cibarius*
		Coprinus quadrifidus
		Dacrymyces deliquescens
		Ganoderma lucidum
		Naematoloma sublateritium
		Pleurotus ostreatus
		Psilocybe cubensis
		Xylobolus frustulatus
Lehrer et al. (1986, 1994)	USA (West, Midwest, Southeast), France, Denmark, Spain, Germany, United Kingdom	*Amanita amara, A. muscaria*
		Armillaria tabescens
		Boletinellus merulioides Boletus sp.
		Calvatia cyathiformis
		Cantharellus cibarius
		Chlorophyllum molybdites
		Coprinus quadrifidus
		Ganoderma meredithae
		G. lucidum
		Geastrum saccatum
		Ishnoderma ludovicianus
		Pisolithus tinctorius
		Pleurotus ostreatus
		Psilocybe cubensis
		Scleroderma sp.
Butcher et al. (1987)	USA (Southeast, Northwest)	*Agrocybe amara*
		Amanita muscaria
		Armillariela tabescens
		Boletus sp.
		Calvatia cyathiformis
		Chlorophyllum molybdites
		Coprinus quadrifidus
		Ganoderma lucidum
		Geastrum sacatum
		Pisolithus tinctorius
		Psilocybe cubensis
		Scleroderma sp.
		Pleurotus ostreatus

Table 3 continued

Author (year)	Place	Basidiomycetes tested
Liengswangwong et al. (1987)	USA (Southeast)	*Armillaria tabescens*
		Calvatia cyathiformis
		Chlorophyllum molybdites
		Coprinus quadrifidus
		Pleurotus ostreatus
		Pisolithus tinctorius
		Scleroderma sp.
Sprenger et al. (1988)	USA (Northwest)	*Agrocybe amar*
		Amanita muscaria
		Armillaria tabescens
		Boletinelus merulioides
		Boletus spp.
		Calvatia cyathiformis
		Cantharellus cibarus
		Chlorophyllum molybdites
		Coprinus quadrifidus
		Ganoderma lucidum
		Inonotus ludovicianus
		Pisolithus tinctorius
		Pleurotus ostreatus
		Psilocybe cubensis
		Scleroderma sp.
Ibañez et al. (1988)	USA (Southeast)	*Calvatia cyathiformis*
		Geaster saccatum
		Pisolithus tinctorius
		Scleroderma aerolatum
Horner et al. (1988, 1991, 1993a, b; 1995)	USA (Southeast)	*Calvatia cyathiformis*
		Ganoderma applanatum
		G. lucidum, G. meredithae
		Pleurotus ostreatus
		Lentinus edodes
Oneil et al. (1988, 1990)	USA (Southeast)	*Armillaria tabescens*
		Calvatia cyathiformis
		Coprinus quadrifidus
		Pisolithus tinctorius
		Pleurotus ostreatus
		Scleroderma sp.
Wongtim et al. (1993)	USA (Southeast)	*Calvatia cyathiformis*
		Pleurotus ostreatus
		Psilocybe cubensis
Helbling et al. (1993a, b, 1998, 1999, 2002)	USA (Southeast), Switzerland	*Boletus spp.*
		Coprinus spp.
		Pleurotus spp.
		Psilocybe cubensis
Brander et al. (1999a, b)	Switzerland	*Coprinus comatus*
Torricelli et al. (1997)	Switzerland	*Agaricus bisporus*
		Boletus edulis
		Coprinus comatus
Rivera-Mariani et al. (2011a, b)	Puerto Rico (Caribbean)	*Airborne basidiospores*
		Airborne ascospores

presence of these fungi in various settings and that exposure and sensitization to other fungi (e.g., mitosporic fungi) has been reported to be risk for asthma (Delfino et al. 1996, 1997; Black et al. 2000; Bush and Portnoy 2001; Semik-Orzech et al. 2008), epidemiological studies are needed to determine the role of airborne spores of basidiomycetes and meiotic forms of ascomycetes in indoor and outdoor environments with exacerbations of respiratory and allergic diseases in geographic areas in which they are predominant, such as in the tropics.

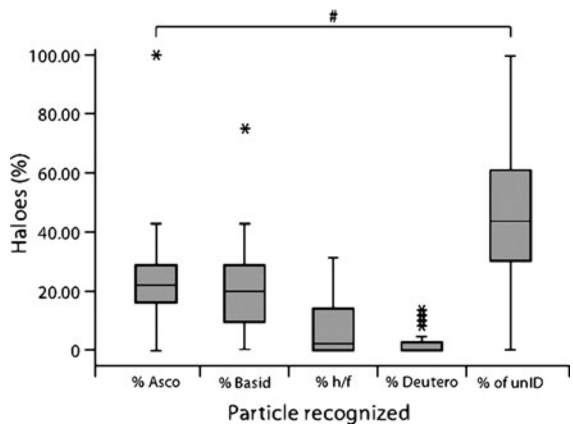

Fig. 4 Percentage of human sera that reacted with each category of airborne fungal particles. Airborne fungal particles were collected and, with the halogen immunoassay, eluted allergens were immunostained with human sera from subjects with allergic respiratory diseases in San Juan, Puerto Rico (Caribbean). Halo refers to the immunostained complex of eluted allergen with human sera. Asco (ascospores), basid (basidiospores), h/f (hyphae and fragments), deutero (deuteromycetes/mitosporic fungi), and unID (particles not able to be identified. $^{\#}p < 05$. Rivera-Mariani et al. (104); reprinted with permission from the publisher S Karger AG

Another aspect requiring further studies are the immunology and molecular biology of these fungi. Antibodies specific to mitosporic fungal allergens have been previously reported in numerous studies (Horner et al. 1995; Green et al. 2003, 2006, 2009; Mari et al. 2003; Horner et al. 2008), but limited investigations in these fields have been performed with basidiomycetes and meiotic forms ascomycetes. In addition, to our knowledge, there are no studies describing the response of cells from the innate (e.g., neutrophils, eosinophils, dendritic cells, etc.) and adaptive (T-cells, B-cells, etc.) immune system to spores of basidiomycete and meiotic forms of ascomycetes and extracts with respect to allergy and asthma. Research on the interaction between these fungi and the different branches of the immune system are needed to better understand the immunological events that take place once susceptible individuals are exposed.

In summary, here we discuss the literature available with respect to the role of basidiomycetes and ascomycetes in respiratory allergies. Compared with mitosporic fungi and other allergens, the current information is very limited. A few studies have been conducted, primarily in the tropics where basidiomycetes and ascomycetes predominate in the atmosphere,

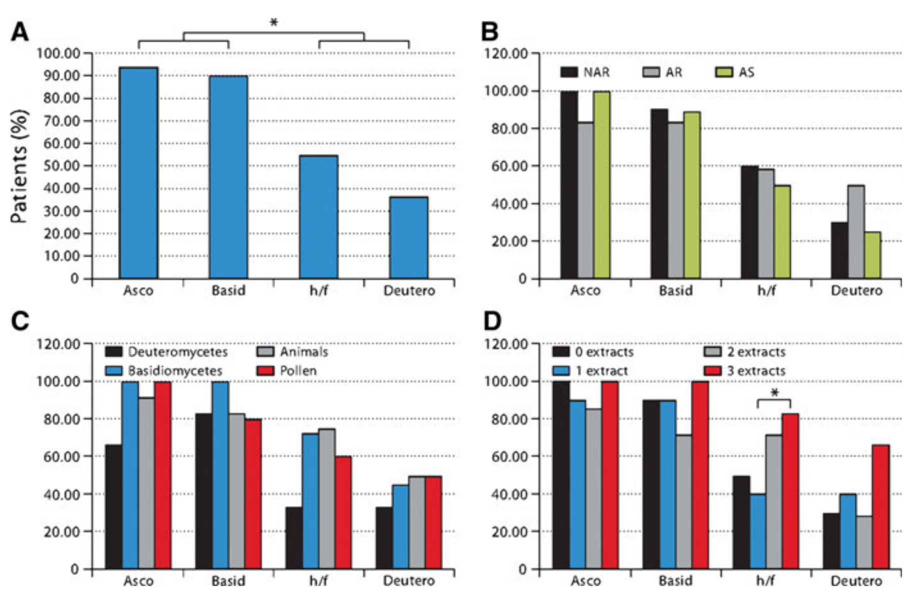

Fig. 5 Percentages of subjects that reacted to fungal particles. **a** All subjects tested (33); **b** according to disease; **c** according to the skin-prick test reactivity of the subjects; **d** according to the number of skin-prick test positive extracts of the subjects tested. AR (allergic rhinitis), AS (asthma), NAR (nonallergic rhinitis), Asco (ascospores), basid (basidiospores), h/f (hyphae and fragments), deutero (deuteromycetes). $^{*}p < 05$. Rivera-Mariani et al. (104); reprinted with permission from the publisher S Karger AG

but some investigations in temperate areas have been performed. Contrary to allergens of plant, food, and animal origins, allergenic proteins fully characterized for basidiomycetes are limited to five genera and none to meiotic forms ascomycetes. It is difficult to diagnose fungal allergies when the principal allergens in an area are not part of routine allergen testing. This could lead to incorrect diagnosis of allergies and treatment strategies not appropriate for the causative allergen. For these reasons, it is important to further study their role in exacerbations of allergies and asthma. There is no doubt that given their predominance in the atmosphere of different countries and studies that have described their allergenic potential, epidemiological, immunological, and molecular biology studies are warranted in order to expand the knowledge about these fungi and their role allergic respiratory diseases.

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