

Minireview: Biological factors causing allergic diseases of occupational origin. Part I: Respiratory disorders

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Much less is known about high-molecular weight allergens of biological origin causing occupational diseases than is known about low-molecular weight naturally-derived or synthetic allergens. Thus, we feel that matching of the most important respiratory diseases against living organisms grouped into 4 taxonomic kingdoms could be useful in the search for aetiological agents causing respiratory disease(s) in particular occupational environments. Two respiratory disorders are considered here: hypersensitivity pneumonitis [HP], a deep lung inflammation that is predominantly an occupational disease evoked by various protein and glycoprotein allergens, and bronchial asthma [BA], a chronic inflammatory disease of the lower airways that is occupational in only 5-15% of all asthma cases and is caused by high-molecular-weight allergens, often in the 20-50 kDa range (Lacey & Dutkiewicz 1994).

Disease: Hypersensitivity pneumonitis [HP]

Kingdom: Bacteria (Eubacteria). Various species of bacteria, mostly those living as saprophytes on grain, wood, and other plant materials and released into the air during processing of these materials, are common causative agents of HP, usually appearing as an occupational disease. Most of the pathogenic bacterial species belong to three phyla: Actinomycetota (Gram-positive bacteria previously known as Actinobacteria), Bacillota (Gram-positive bacteria previously known as Firmicutes), and Pseudomonadota (Gram-negative bacteria previously known as Proteobacteria). Members of the Actinomycetota – filamentous, mostly thermophilic (developing at high temperatures) bacteria – and the Bacillota can cause known subtypes of HP: *Saccharopolyspora rectivirgula* and *Thermoactinomyces vulgaris* cause “farmer’s lung” due to exposure to overheated hay, grain or other plant materials (Selman et al. 2012, Greenberger 2019, Nogueira et al. 2019); *Thermobifida fusca* causes “mushroom compost producer’s lung” due to exposure to overheated compost (Mackiewicz et al. 2026), and *Laceyella sacchari* (previously named *Thermoactinomyces sacchari*) causes bagassosis due to exposure to bagasse (sugarcane residue) (Selman et al. 2012, Riario Sforza & Marinou 2017). *Streptomyces* spp. [Actinomycetota; mesophilic (developing at moderate temperatures), filamentous actinomycetes occurring commonly in plant and soil dust] may cause HP in farmers and

gardeners (Dutkiewicz 2010). The Actinomycetota comprise also non-filamentous, rod-shaped, mesophilic Gram-positive organisms of which such species as *Arthrobacter globiformis* and *Brevibacterium linens* present in grain dust (Milanowski et al. 1998) and *Microbacterium betulae* present in wood dust (Paściak et al. 2024) cause HP in exposed workers. To this phylum belong also mycobacteria, of which *Mycobacterium immunogenum* and *M. avium* developing in cutting oils cause a HP entity named “machine operator’s lung” (Selman et al. 2012, Nogueira et al. 2019). Among the Pseudomonadota, the most important HP-causing agent is *Pantoea agglomerans*, a Gram-mesophilic negative rod, widespread in nature, mostly on grain and wood, causing “thresher’s lung” (Dutkiewicz et al. 2016) and HP in woodworkers (Mackiewicz et al. 2019). HP may be caused also by other Gram-negative bacteria, such as *Alcaligenes faecalis* occurring in grain, hay and herbs (Milanowski et al. 1998).

Kingdom: Fungi. Microfungi described as moulds have often been described as a cause of HP. Most of them belong to the genera *Aspergillus* [*A. clavatus* (now named *Neosartorya clavata*), *A. fumigatus*, *A. terreus*, *A. umbrosus*, *A. versicolor* (now named *Emericella versicolor*)] (Dutkiewicz 1998) and *Penicillium*, including *P. glabrum* (previously named *P. frequentans*) causing suberosis in cork processing workers (Greenberger 2019) as well as *P. casei* (now named *P. verrucosum*), *P. roqueforti* and *P. camemberti* causing “cheese washer’s disease” (Frazier 1980). Moulds from other genera may also induce HP, such as *Rhizopus microsporus* (syn. *Rhizopus microsporus* var. *rhizopodiformis*) in Scandinavian woodworkers (Dutkiewicz et al. 2007). The common budding yeast (*Saccharomyces cerevisiae*) was identified as a cause of HP in a farmer (Dutkiewicz 2006). HP could be evoked also by exposure to button mushroom (*Agaricus bisporus*) and oyster mushroom (*Pleurotus ostreatus*) spores in mushroom growers (Dutkiewicz 2006).

Kingdom: Plants (Plantae). With few exceptions, plants themselves are rarely reported as causative agents of HP. An exception may be *Stipa tenacissima*, esparto grass, which has been described as causing stipatosis an occupational disease seen in those working with esparto fiber used for the manufacture of ropes, hemp sandals, rush mats, etc. The mould *Aspergillus fumigatus* has also been implicated (Hinojosa 2001, Moreno-Ancillo et al. 2003, Riario Sforza & Marinou 2017).

Kingdom: Animals (Animalia). The most important HP subtype is “bird fancier’s lung” caused by the inhalation of dust contaminated with birds’ epithelia, faeces, and feathers, mostly originated from pigeons and budgerigars kept by hobbyists, less frequently from hens, ducks, turkeys, and pheasants (Dutkiewicz 1992). There is only little evidence implicating allergens originating from mammals and from arthropods as a cause of HP.

Disease: Bronchial Asthma (BA)

Kingdom: Bacteria (Eubacteria). Bacteria have long been thought to play a significant role in triggering or worsening intrinsic asthma (caused by strains developing in the human body; see Tian et al. 2024), but little is known about the role of bacteria in causing extrinsic asthma evoked by allergens present in external air, including those in occupational premises.

Kingdom: Fungi. Moulds belonging to the genera *Aspergillus* (*A. flavus*, *A. fumigatus*), *Penicillium* and other genera (*Alternaria* spp., *Chaetomium*, *Cladosporium*) are a frequent cause of asthma in agricultural workers (Dutkiewicz et al. 2007). Asthma in farmers may be induced also by fungi parasitising wheat, for example *Puccinia graminis*, *Ustilago* spp. and *Tilletia* spp. (Dutkiewicz et al. 1988, Dutkiewicz 1992, Dutkiewicz 1998, Dutkiewicz et al. 2007). Enzymes of *Aspergillus oryzae* and *Aspergillus niger*, as well as of the common budding yeast (*Saccharomyces cerevisiae*) used in the baking industry, may lead to occupational asthma in bakers (Dutkiewicz 2006, Dutkiewicz 2010).

Kingdom: Plants (Plantae). In contrast to HP, plant particles represent a common cause of BA. Asthma may be caused by work-related inhalation of dust released during processing of various crop plants (tea, coffee, rice, buckwheat, soya, castor bean), vegetables (artichoke, asparagus, dill, garlic, pea), spices (thyme, rosemary, cinnamon, anise, sesame) as well as industrial and forage plants (rapeseed, sunflower, lupine, poppy) (Frazier 1980, Dutkiewicz 2006). There are also reports describing cases of occupational BA after respiratory exposure to pulverised tissues of plants used as medications, such as narrowleaf plantain (*Plantago lanceolata*) or ipecacuanha (*Carapichea ipecacuanha*) (Dutkiewicz 2006), as well as after exposure to dust plant proteases used in the food industry, for example papain from papaya fruits or bromelain from pineapple fruits (Frazier 1980, Dutkiewicz 2006). Dust from flowers, such as chrysanthemums, cloves, roses, tulips, hyacinths, lilies and freesias may cause occupational asthma in about 8% of greenhouse flower and ornamental plant growers (Monsó et al. 2002). Even more hazardous is exposure to wood dust that may be a cause of asthma in 6-18% workers (Baatjies et al. 2023).

Kingdom: Animals (Animalia). Allergens of poultry (epithelia, feathers, faeces) may cause asthma among breeders (Bar-Sela et al. 1984), whereas hen egg proteins cause this disease in workers processing egg mass (Dutkiewicz 1998). However, in contrast to HP, BA may occur in a wide range of occupations under respiratory exposure to other vertebrates and to invertebrates. Thus, asthma in farmers breeding mammals may be caused by allergenic proteins present in pig urine as well as in cow hair and dander (Dutkiewicz 1998). Workers breeding rats and mice in scientific laboratories are at risk of acquiring "laboratory animal allergy" (LAA) caused by exposure to an aerosol of urine or dander of bred rodents (Bush & Stave 2003). Asthma cases were described in workers exposed to fish meal and to a droplet aerosol from processed salmon protein (Dutkiewicz 2006). BA cases were also described among workers producing sea food from marine invertebrates: mussels, crabs and cephalopods (Frazier 1980, Dutkiewicz 2006). Finally, exposure of people working in stores of agricultural products are under risk of "storage mite asthma" caused by the inhalation of faeces and body particles of small (0.3-0.75 mm) mites feeding on stored products: *Acarus siro*, *Tyrophagus putrescentiae*, *Lepidoglyphus destructor*, and *Glycyphagus domesticus* (Ingram et al. 1979).

Conclusion

The occurrence of the type of occupational allergy (hypersensitivity pneumonitis - HP or bronchial asthma - BA) depends to a large extent on the qualitative classification of allergen-producing organisms. Allergens produced by bacteria usually cause HP, very rarely BA. By contrast, allergens of plant and animal origin (except for those produced by birds) usually cause BA and rarely HP. The only organisms that seem to cause HP and BA to similar extent are fungi and the aforementioned birds.

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