PRIMEVIEW

HYPERSENSITIVITY PNEUMONITIS

nature reviews disease primers

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Hypersensitivity pneumonitis (HP) is a syndrome caused by the inhalation of a variety of environmental antigens in susceptible and sensitized individuals. Common antigens include bird proteins, fungi, plant proteins and chemicals in paint or plastic.

DIAGNOSIS

The distinction between fibrotic and non-fibrotic forms of HP is important as fibrotic features are associated with worse outcome. Chronic HP results from long-term, low-level exposure and results in non-specific symptoms such as cough, dyspnoea and fatigue; the lack of or unnoticed acute 'flares' often leads to misdiagnosis of patients. By contrast, acute HP is attributed to intermittent, high-level exposure to the inducing antigen; symptoms occur abruptly (within hours after exposure) and patients experience influenza-like symptoms.

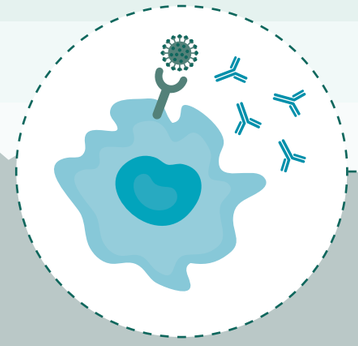
! HP also has different names, depending on the provoking antigen; 'farmer's lung' is HP caused by exposure to mouldy hay or straw, whereas 'bird breeder's lung' is HP caused by exposure to bird proteins

PREVENTION

Diminishing or avoiding exposure to inciting antigens is essential to prevent HP. Routine inspections to identify potential sources of antigens in bioaerosols in the work place and in homes, use of personal protective equipment and disinfection or sterilization (for example, for fungi) can also be effective to reduce exposure.

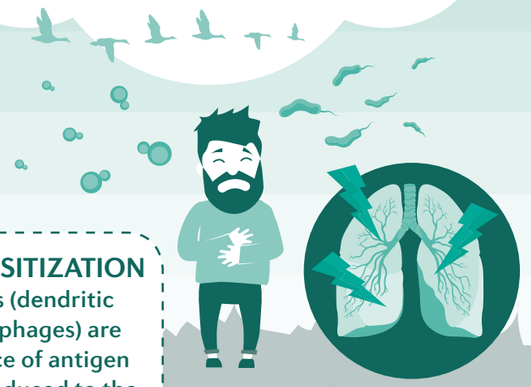
MECHANISMS

Genetic and host factors may explain why only few individuals develop HP; the exact mechanisms are not fully known but seem to involve many factors



EXPOSURE AND SENSITIZATION

Antigen-presenting cells (dendritic cells and alveolar macrophages) are activated by the presence of antigen and antibody (IgG) is produced to the antigen (sensitization)



SECOND HIT

An additional 'hit' seems to contribute to the development of HP - viruses, pesticides or air pollutants

EXAGGERATED IMMUNE RESPONSE

T helper 1 cells accumulate in the lung, creating a pro-inflammatory microenvironment that is exacerbated owing to impaired suppressive activity of regulatory T cells

FIBROSIS

Ageing, smoking and autoimmune features may contribute to the progression to lung fibrosis

! Changes in the immune response (favouring T helper 2 cells and loss of FOXP3 expression by regulatory T cells) as well as overexpression of several profibrotic molecules also contribute

MANAGEMENT

Antigen avoidance is the mainstay of treatment. Most acute episodes of HP are self-limited, and patients recover after antigen removal. Immunosuppressant corticosteroids are often used, but the evidence supporting this approach is scant. In fibrotic HP, the optimal management is not well established. In these patients, glucocorticoids, other immunosuppressive therapies (such as azathioprine, mycophenolate mofetil or rituximab) or antifibrotic drugs (such as nintedanib and pirfenidone) have been used. Lung transplantation can be considered in patients with progressive chronic fibrotic HP.

OUTLOOK

New antigens are constantly identified that can lead to the development of HP. Accordingly, a central 'register' of these antigens with case descriptions would be useful for ongoing research. Additional research efforts are needed to determine the mechanisms leading to sensitization, and why disease develops only in a minority of exposed individuals; genome-wide association studies may help to identify genetic risk factors.

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