Annex I 304.01

Extrinsic allergic alveolitis

Definition of causal agent

Extrinsic allergic alveolitis EAA (also known as hypersensitivity pneumonitis HP) comprises a group of related inflammatory interstitial lung diseases that result from hypersensitivity immune reactions to the repeated inhalation of various antigens derived from fungal, bacterial, animal protein, or reactive chemical sources.

or

Extrinsic allergic alveolitis EAA (also known as hypersensitivity pneumonitis HP) is an inappropriate immune response to inhaled antigens that causes shortness of breath, a restrictive lung defect, interstitial infiltrates seen on lung imaging [chest X ray and high-resolution computed tomography (HRCT)] due to the accumulation of large numbers of activated T lymphocytes in the lungs.

Main occupational uses and sources of exposure:

HP results from inhalation of organic dust or some reactive chemical substances. The examples of causal agents and related diseases are listed in the annex. The list is an open one.

Toxic effects

Annex

Antigen source	Probable antigen	Disease
	Microorganisms and plants	
Mouldy hay	*Saccharopolyspora rectivirgula* *Thermoactinomyces vulgaris* *Aspergillus sp.* *Penicilium sp.* *Wallemia sebi* *Fusarium sp.*	Farmer's lung disease
Mouldy pressed sugarcane	*Thermoacntinomyces sacchari* *Thermoactinomyces vulgaris*	Bagassosis
Mouldy compost and mushrooms	*Thermoactinomyces vulgaris* *Saccharomyces rectivirgula* *Aspergillus sp.* *Penicillium sp.* Mushroom spores	Mushroom worker's disease

Mouldy cork	*Penicillium sp.* *Aspergilus sp.* Cork	Suberosis
Contaminated barley	*Aspergillus clavatus*	Malt worker's lung
Contaminated wood pulp	*Alternaria sp.*	Wood pulp worker's disease
Contaminated wood dust	*Bacillus subtilis* *Alternaria sp.* Pine sawdust	Wood dust HP
Mould on tobacco	*Aspergillus* sp.	Tobacco worker's disease
Mould on grapes	*Botrytis cinerea*	Wine grower's lung
Cheese or cheese casings	*Penicillium* sp.	Cheese worker's disease
Esparto grass *(Stipa tenacissima)* used to produce plaster	Esparto grass antigens Thermophilic actinomycetes *Saccharopolyspora rectivirgula* *Aspergillus* sp.	Stipatosis
Biomass in air-conditioning system	*Cytophaga* (gram-negative bacteria)	Nylon plant lung
Contaminated humidifiers, air conditioners, heating systems	*Thermoactinomyces candidus* *Thermoactinomyces vulgaris* *Penicillium* sp. *Cephalosporium* sp. *Candida* sp. Amoebe *Klebsiela* sp.	Ventilator lung Humidifier lung
Contaminated metal working fluid	*Pseudomonas* sp. *Acinobacter* sp. *Mycobacterium* sp.	Metal working fluid HP
Contaminated tractor cab air conditioner	*Rhizopus* sp.	Tractor lung
Grain weevils in wheat flour	*Sitophilus granarius* protein	Miller's lung
Animals		
Silk worm larvae	Silk worm larvae proteins	Sericulturists's lung
Rat urine	Rat urine protein	Laboratory worker's HP
Pigeon droppings	Pigeon proteins	Pigeon breeder's disease
Chicken feathers	Chicken feather proteins	Chicken breeder's lung
Chemicals		
Toluene diisocyanate (TDI)	Altered proteins	TDI HP
Diphenylomethane diisocyanate (MDI)	Altered proteins	MDI HP
Hexamethylene diisocyanate (HDI)	Altered proteins	HDI HP
Trimellitic anhydride (TMA)	Altered proteins	TMA HP

Diagnostic criteria:

There is no single diagnostic or clinical laboratory test available to diagnose HP. Diagnosis is made from a combination of characteristic symptoms, physical findings, X-Ray abnormalities, pulmonary function and immunological tests. Confirmation of exposure to the inciting antigen can be obtained

by history, environmental inspection, serum precipitins and/or bronchoalveolar lavage fluid antibodies

☐ History

Symptoms consistent with AA that appear or worsen within hours after antigen exposure.

☐ Clinical

Acute form: chills, dyspnea, cough, chest tightness, malaise, fever, bilateral inspiratory crackles occurring 3-8 hours after beginning of exposure

Subacute form: progressive increasing shortness of breath, cough which is generally dry, weight loss, inspiratory crackles.

Chronic form: progressive dyspnea, fatigue, anorexia, weight loss, chronic cough often with sputum production, crackles, rhonchi, 'squawks"; in very advanced cases, signs of cor pulmonale.

☐ Lung function

Restrictive ventilatory pattern and a decreased diffusing capacity for carbon monoxide; a mild obstructive pattern is sometimes observed. Arterial blood gas analysis usually shows hypoxemia of variable degree.

☐ Immunological Findings

Serum: presence of precipitating immunoglobulin (IgG) antibodies against offending antigen.

Bronchoalveolar lavage (BAL): a marked lavage lymphocytosis is found. The lymphocytes are predominantly of the T-suppressor subtype (CD8+) and the ratio CD4+/CD8+ is generally less than 1. Increased BAL neutrophils are observed shortly after antigen exposure.

☐ Inhalation Challenge

The use of inhalation challenge in the diagnostics of AA is limited by the lack of standardized antigens and techniques. This test is not essential for diagnosis.

☐ Histopathology

Histologic triad – (i) cellular infiltrates of lymphocytes and plasma cells along airways, (ii) interstitial infiltrates of lymphocytes and plasma cells, (iii) single, non-necrotizing granulomata in the parenchyma with some in bronchiolar and alveolar walls, but without mural vascular involvement.

☐ Radiology

HRCT is the most useful imaging tool to evaluate AA.

Acute form: Normal or diffuse or patchy air-space consolidation

Subacute form: centrilobular nodules or widespread nodular opacities and ground-glass attenuation

Chronic form: Mid –lung zone fibrosis, honeycombing.

Differential diagnosis :

1. organic dust toxic syndrome
2. infectious pneumonitis
3. lymphocytic leukemia
4. sarcoidosis
5. chronic beryllium disease
6. drug-induced interstitial lung disease
7. bronchiolitis obliterans with organizing pneumonia
8. all types of chronic diffuse pulmonary fibrosis

Exposure criteria:

Minimum intensity of exposure: Although the symptoms usually appear with high concentrations of the antigen in the working environment, there is no good relationship between dose and effect.

Maximum duration of exposure: from few minutes to few months.

Maximum latent period: - acute form: 8 hours
- subacute form: 8 days
- chronic form: one year