Occupational Airways

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This issue:

⇒ Hypersensitivity Pneumonitis (HP)
⇒ Some Clinical Observations about Interstitial Lung Disease (ILD) in CT
⇒ Summary Table of Reported Cases of Selected Respiratory Diseases in

HYPERSENSITIVITY PNEUMONITIS (HP)

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Hypersensitivity pneumonitis (HP), also called extrinsic allergic alveolitis, is a granulomatous interstitial lung disorder resulting from reaction to repeated inhalations of and sensitization to allergens in a predisposed host.[1] Occupationally, it occurs in susceptible workers, and is an immunologically mediated inflammatory response in the alveolar-air exchange portions of the lung, rather than in the conducting airways as in occupational asthma.

It was first described as a clinical entity by Ramazzini in 1713 with the symptoms of cough and shortness of breath in workers exposed to dusts of over-heated cereal grains. Campbell[2] first described Farmer's Lung in 1932, which was further defined by Dickie and Rankin[3] in 1958 as an acute granulomatous interstitial pneumonia caused by exposure to moldy hay.

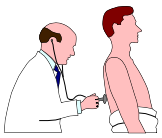
The well described criteria for diagnosis of HP as outlined by Fink, Lindermith and Horvarth in Lenz's Occupational Medicine textbook[4] will be utilized to describe this clinical disorder.

1. History of exposure to a recognized antigen

There is a long list of antigens known to precipitate this disorder. They include various microorganisms, serum proteins and chemicals. Table 1 includes a number of entities and offending allergens more likely to be seen in Connecticut. Not as common in Connecticut but well described in the literature are bagassosis in sugar cane workers, sisal worker's disease, maple bark stripper's disease, wheat weevil's disease and malt worker's lung.

2. Symptoms of fever, cough and shortness of breath

The symptoms occur in a spectrum, from acute through chronic stages. Two-thirds develop chills, fever, cough and shortness of breath within four to eight hours after exposure, which develop into symptoms of malaise, myalgia and headache. Initial symptoms usually subside within hours. The sub-acute phase is represented by a decrease in the acute symptoms but progressive increase in shortness of breath. The chronic phase is characterized by progressive shortness of breath, and with features of both an interstitial and airways obstruction disorder. A careful occupational history is essential in evaluating the patient presenting with these symptoms.



The physical examination during the acute phase usually notes a moderately ill appearing patient, dyspneic, occasionally cyanotic, with bi-basilar rales. Rarely there is wheezing. In the sub-acute and chronic phases the bi-basilar rales remain prominent, as does the presence of dyspnea.

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Table 1[4,5,6,7,8]
Potential Sources of Hypersensitivity Pneumonitis in CT

Disease	Workers	Source	Antigen
Farmer's Lung[4,5,6,7,8]	Dairy Farmers	Moldy Hay	*Micropolyspora faeni*
Mushroom Worker's Lung[4,5,6,7,8]	Mushroom workers	Compost	Thermophilic actinomycetes
Tobacco Worker's Lung[8]	Tobacco workers	Mold on tobacco	*Aspergillus spp.*
Ventilation Pneumonitis[5,6,7] Humidifier Lung[4,5,6,8] Air Conditioner Lung[5]	Office workers	Water reservoirs	Multiple organisms
Bird Breeder's Lung[5,6,7]	Bird breeders, handlers	Bird droppings, feathers	Avian proteins
Laboratory Technician's Lung[7]	Lab Animal handlers	Rat urine	Rat urine proteins
Machine Operator's Lung[8]	Metal workers	Aerosolized metal-working fluid	Multiple organisms
Isocyanate Disease[4,5,6]	Paint sprayers Foam insulators	Paints, resins, polyurethane foams	Toluene diisocyanate (TDI)* Diphenylmethane diisocyanate (MDI)* Hexamethylene diisocyanate (HDI)*
Phthalic anhydride Lung Disease[4,6,]	Epoxy resin workers Plastic workers	Resins, plastics	Phthalic anhydride
Trimellitic anhydride Lung Disease[5,6]	Plastic workers, surface coating manufacture	Plastics, resins, paints	Trimellitic anhydride

*Also known asthmagens

3. Pulmonary function changes

During the early phase of the disorder there is early air trapping with an increase in residual volume, a decrease in vital capacity (representative of the restriction changes in the lung), a decrease in compliance (representing the stiffness of the lung), but usually a normal airway resistance. With progression of the abnormalities in imbalance in ventilation-perfusion relationships due to the pathology of the disorder, hypoxemia will be evident. A decrease in diffusion capacity is also commonly seen. Early in the development of the entity, there may be a decrease in FEV_1 (Forced Expiratory Volume). However, this is usually fleeting, and the classic changes seen in obstructive disease are not prominent. The pulmonary function changes associated with the chronic stage of the disorder are those of combined obstructive airways and diffuse interstitial fibrosis. The hypoxemia seen in the early stage of the disorder may be severe and even life-threatening.

4. Chest x-ray changes

The characteristic x-ray change is that of interstitial reticulonodular densities up to several millimeters in size, which are especially basilar in distribution. These x-ray changes clear slowly over weeks to months. Occasionally the nodular densities will be widely scattered throughout the lung parenchyma, producing a "white-out" pattern, however this is less common. In cases of multiple allergen exposure, the fibrotic densities clear very slowly, or may not clear at all. It is important to note that the x-ray may be normal in cases of HP, even with a positive biopsy. X-rays have been shown to be normal in many outbreaks of HP[9]. Therefore, physicians have increasingly relied upon high resolution computed tomography (HRCT) scans. Nevertheless, even HRCT appear to be normal in 50% of biopsy proven HP cases, so physicians should be fairly aggressive about documentation of disease.

5. Evidence of immunological sensitization

In 1965, Pepys described the development of precipitins against thermophilic actinomyces in Farmer's Lung.[10] Much work has been carried out related to the immunology of HP. It was first considered to be a type III immune complex mediated reaction. However, the current feeling is that it is a cell-mediated mechanism produced by alveolar macrophages, T-lymphocytes, NK cells, and cytokines. It appears that there is an activation of multiple mechanisms upon allergen exposure with resultant expansion of T-cell clones and generation of granulomatous and fibrogenic factors, leading to parenchymal damage.

A majority of individuals exposed to an inhalant antigen do develop a cellular and humoral response. However, only a small percentage, possibly 3-15%, go on to develop disease. Precipitins may develop in up to 50% of subjects exposed to an allergen without any evidence of disease. This makes the use of precipitin testing in diagnosis of the disorder of questionable value, because of the number of resultant false positives. Therefore, precipitating antibodies are useful primarily as indicators of *exposure* rather than of disease.[11]

Factors other than specific immunological reactions are considered to be operational in the pathogenesis of this disorder. Those presently under consideration are host factors such as genetics, endotoxins, infection, and various toxic factors such as air pollution and even cigarette smoke, which may protect against the development of this disorder.

Enzyme linked immunoabsorbent serum assay (ELISA) may be used in the laboratory diagnosis of the disorder, instead of the double immunodiffusion technique originally used. Though, it may have an excess number of false positives, as previously discussed. In addition, most of the fungal antigens that cause this disorder are only very poorly characterized, and linking antigen extracts has been difficult at times.

The remaining criteria are to be utilized only in selected cases.

6. Provocation inhalation challenge

This is rarely necessary, unless the offending allergen is not a well-recognized one. It is only to be done in a laboratory well equipped in the Williams technique. It is much better to note clinical change in the patient by workplace exposure manipulation.

7. Pulmonary biopsy

The characteristic changes are those of a monocellular interstitial pneumonitis, with alveolitis, granulomas, intra-alveolar "buds", and interstitial fibrosis in the alveolar walls, with lymphocytes scattered throughout the fibrotic areas being especially noted.

8. Bronchial lavage

Bronchial lavage will help distinguish this entity from other interstitial lung diseases by the presence of a large number of lymphocytes, instead of an increase in granulocytes as seen in others. The characteristic lavage findings are high lymphocyte count, high percentage of CD8 or suppressor types, increase in total protein, increase in IgG/albumen ratio, presence of cytokines, and possible IgM and IgG antibodies.

Prevention and Treatment

The cornerstone of prevention is avoidance of exposure. In acute and sub-acute cases, resolution is usually spontaneous without specific treatment. In most cases, removal from exposure and supportive treatment is all that is indicated. In severe cases with life-threatening hypoxemia, corticosteroids may reverse the disease, and would be indicated.

Removal of an exposed worker from the workplace may be disruptive, but is medically necessary. If this is not possible, all attempts must be made to keep the exposure to as low a level as possible. Altering the engineering process is the best solution. Such engineering changes have been particularly successful in bagassosis, office humidifier lung disease, farmer's lung, and maple bark stripper's lung. Well developed education of workers and industries at risk is also of importance in prevention.

For further information, contact Dr. Kent at 860/535-3654.

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Summary of Number of Reported Cases of Selected Respiratory Diseases in CT

CT DPH Occupational Disease Surveillance Data

	1994	1995	1996	1997*	ODSS Total**
Asthma	13	34	33	18	139
RADS* **	1	1	5	3	16
Silicosis	4	1	0	1	8
Asbestosis	3	5	10	2	47
Asbestos-related pleural diseases	17	8	7	2	125
Total	38	49	55	26	335

* As of October 31, 1997. Data subject to change.
** Occupational Disease Surveillance System (ODSS) total since 11/91
*** Reactive Airways Dysfunction Syndrome

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TO:

Some Clinical Observations about Interstitial Lung Disease (ILD) in Connecticut

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Interstitial lung disease (ILD) represents a broad group of disorders with the common endpoint, fibrosis. Hypersensitivity pneumonitis (HP), as the prototypical modern occupational and environmental pulmonary disorder, represents only approximately 1.5% of these disorders. Nevertheless, work in the U.K.[1,2] and in Connecticut[3] has demonstrated associations between non-granulomatous ILD and exposure to metals, organic solvents, and wood and vegetable dusts. A similar association was recently suggested for sarcoidosis[4] in a public health masters thesis at the University of Connecticut. This raises the question whether other ILDs besides HP, asbestosis, and silicosis are work-related and preventable.

Machining and metal work exposure has been of interest in the occupational lung disease community for some years because of an outbreak of hypersensitivity pneumonitis.[5] A recent review outlines our current knowledge. A project funded jointly by General Motors and the United Autoworkers Union has led to the publication of five papers in the last six months on the relationship of endotoxin exposure and non-specific lung function changes.[6] An ongoing outbreak investigation in central Connecticut is being examined in detail collaboratively by scientists throughout New England. This reinforces the association of metals (or metal working fluids) exposure with ILD as shown in case-control studies. Given the importance of metalworking in CT, physicians should be aware of this potential cause.

Moisture has been the primary cause of HP in large buildings for many years.[7] A recent outbreak of sarcoidosis in a Connecticut school associated with acute restrictive lung function changes and outbreaks of non-granulomatous lung disease suggest, together with metal working fluids, that environments and exposures classically associated with HP may give rise to other forms of ILD.

Large, nationally representative case control studies of non-granulomatous ILD and of sarcoidosis are underway. They may shed more light on these associations. ILDs represent sentinel health events. Occupational histories for pertinent exposures are *always* appropriate. Others in the same facilities may be exposed and also have disease. Remediated exposures may prevent the progression of disease.

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