

Environmental challenge: An effective approach for diagnosis and remediation of exacerbations of hypersensitivity pneumonitis



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Clinical Implications

- An environmental avoidance challenge procedure, which may take several weeks for a response, is a critical tool in evaluating idiopathic interstitial lung disease to establish a diagnosis of hypersensitivity pneumonitis, identify a causative environment, and determine effective remediation.

TO THE EDITOR:

Hypersensitivity pneumonitis (HP) is an inflammatory lung disorder caused by the inhalation of an organic antigen in predisposed patients. Activation of the immune system, directed toward the antigen, leads to recruitment of inflammatory cells resulting in insult to respiratory dynamics. There are 3 temporal patterns of HP based on the history of symptoms and the course of the disease: acute, subacute, and chronic.¹ Exacerbations may occur in all 3 forms depending on levels of exposure.¹ Many cases can quickly be diagnosed using somewhat antiquated criteria.^{2,3} Effective remediation, or avoidance, can be undertaken and a favorable outcome obtained.

Many patients, however, fail to meet enough criteria to establish a clear diagnosis, leading to misdiagnosis or a significant delay in diagnosis. Likewise, with a biopsy consistent with HP, failure to identify a possible causative antigen and environment is very common. Both the above situations may lead to failure to prevent progression of the disorder, causing increased morbidity and mortality.⁴

Here, we present a case, only meeting partial criteria, demonstrating the effectiveness of an environmental avoidance challenge procedure in establishing the diagnosis and in the confirmation of adequate remediation.

A nonsmoking woman, age 75 years, with no history of respiratory tract symptoms was referred after developing a month-long, labored cough and a profound sense of fatigue. She had no wheezing, fevers, night sweats, hemoptysis, or weight loss. Spirometry revealed a reduced forced vital capacity. Computed tomography of the chest showed bilateral apical and upper-lobe infiltrates. A sedimentation rate of 99 mm/h (0–20 mm/h) and a C-reactive protein level of 137 mg/L (0.0–3.30 mg/L) were recorded. Serum precipitins were negative to a panel of *Aspergillus* antigens including *Aspergillus niger*, *Aspergillus fumigatus*, *Aspergillus flavus*, and *A. fumigatus* 1 and 6. A second panel was also negative including pigeon serum, *A. fumigatus* 1 and 6, *Thymus vulgaris*, *Faenia retivirgula*, *Thermoactinomyces candidus*, *Aureobasidium pullulans*, *Saccharomonospora viridis*, and *Thermoactinomyces sacchari*. HP was the tentative diagnosis, and she was advised to move from her home while an environmental investigation was conducted.

The patient lived in a 25-year-old home that was located on a farm; however, she did not participate in any farming activities.

The central forced-air handling system had developed a condensate line blockage 7 to 8 years previously; however, no dust, nor discoloration, was observed on the air conditioning registers. There had been a roof leak located over the living room area nearly 6 months before the patient's onset of respiratory symptoms. The roof was replaced; however, no mold contamination was discovered. She slept on a goose/duck down pillow. A "musty" smell, indicative of volatile organic compounds probably produced by molds, was noted throughout the residence by the patient and others; however, no mold growth was visualized. While the patient was avoiding the home, 2 investigational companies inspected the home, yet neither was able to identify a possible causative factor. Minimal generic remediation suggestions were made and executed, including removal of goose/duck down from the home.

Eleven days after moving from the home, she had only a very mild cough and her energy levels had returned to normal. The lungs were clear; however, the forced vital capacity was slightly abnormal. The sedimentation rate and the C-reactive protein level had returned to normal. She was advised to return to her home to undergo an environmental challenge to determine whether remediation had been effective. She continued to do well with normal energy levels, throat clearing, and a slight cough until reactivation of a labored cough and profound tiredness and fatigue approximately 4 weeks after returning to the home. Rather than, again, moving her from the home, prednisone, 20 mg twice daily, was begun. Further investigation by a family member revealed mold growth around a wall light fixture beneath the area of the roof leak. Upon opening the wall space, heavy mold growth was discovered, but not identified. Remediation was undertaken and completed. Prednisone was tapered, and she was followed for 3 months to ascertain nonprogression (Figure 1).

This case is representative of many patients seen by physicians in which there are minimal criteria for establishing a working diagnosis. Formal pulmonary function testing and bronchoscopy with biopsy were not done. Serum precipitins were negative. Two investigations by industrial hygienists of the home failed to reveal a possible causative antigen, and a generic remediation attempt failed to remove the causative antigen. The environmental challenge back into the home required 27 days of exposure before an exacerbation occurred. All these factors are inconsistent with the current perception of parameters to diagnose and treat HP.

An effective solution to a complex problem revolves around an avoidance challenge procedure.⁵ Moving to a new residence was a successful intervention. After investigations and modest remediation, in which no causative factors were found, the patient returned to the home. Exacerbation of symptoms and inflammatory markers after 27 days of exposure confirmed the home as the causative environment. The most recently published diagnostic criteria³ state that exacerbations should occur within several hours after exposure to the causative environment; however, reports have shown that days to weeks may pass before signs and symptoms recur.^{5–7} Increased inflammatory markers may precede symptoms, changes in spirometry, and radiographic

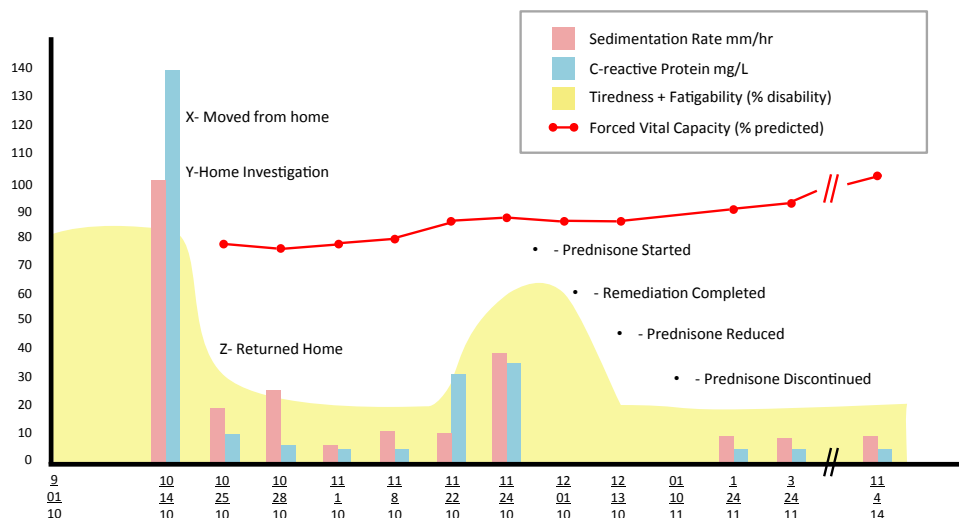


FIGURE 1. Details of the clinical course and environmental avoidance challenge procedure by date. Tiredness and fatigability, as subjectively assessed by the patient, are expressed as percent disability. Upon exacerbation, prednisone, 20 mg twice daily, was begun on November 29, 2010, leading to resolution of symptoms. Remediation was undertaken and completed. Prednisone was tapered on December 13, 2010, to 10 mg twice daily and discontinued on January 13, 2011.

findings, allowing one to intervene before more severe manifestations occur.⁵

An industrial hygienist's investigation may not define a causative factor. The exacerbation, during the environmental challenge, mandated further investigation, ultimately leading to the discovery of a microbial contamination within a wall space beneath a roof leak. Specific remediation of the microbial contamination within the wall space led to nonprogression of the disorder. A long-term follow-up after 4 years revealed a total resolution of signs and symptoms, confirming effective remediation. Partially effective remediation may lead to reduced exposure to the antigen resulting in less intense signs and symptoms, thereby converting the patient from an acute presenter to sub-acute, or chronic.⁵

Conversion to a chronic presentation of HP is dangerous for the patient to develop advanced fibrosis before becoming aware of the insidious progression.

HP was considered an occupational disease in the past. As occupations were recognized as hazardous, safety measures were undertaken to reduce or eliminate the exposure to the causative antigen. Over the past several years, most cases have occurred with at-home exposures.⁸⁻¹⁰ The primary causes are related to lifestyles in different geographic locales and cultures. Dominant causes include (1) avian antigens, either from birds in the home or from goose/duck down bedding; (2) hot tub contaminants; (3) mold in homes; and (4) thermophilic bacteria.

The key factors in confirming HP cases that are difficult to accurately diagnose are persistent, long-term follow-up and continuous assessment of environmental possibilities. The onus is on the long-term managing local physician to continue to question all cases of progressive idiopathic interstitial lung disease. The utilization of an environmental avoidance challenge procedure may be the most effective tool to confirm the diagnosis, to identify the causative environment, and to determine whether remediation has been effective. This approach may

significantly reduce morbidity and mortality of these, otherwise, progressive disorders.

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REFERENCES

- Zacharisen MC, Schlueter DP, Kurup VP, Fink JN. The long-term outcome in acute, subacute, and chronic forms of pigeon breeder's disease hypersensitivity pneumonitis. *Ann Allergy Asthma Immunol* 2002;88:175-82.
- Schuyler M, Cormier Y. The diagnosis of hypersensitivity pneumonitis. *Chest* 1997;111:534-6.
- Patel AM, Ryu JH, Reed CE. Hypersensitivity pneumonitis: current concepts and future questions. *J Allergy Clin Immunol* 2001;108:661-70.
- Dickson SD, Tankersley MS. Fatal hypersensitivity pneumonitis from exposure to *Fusarium vasinfectum* in a home environment: a case report. *Int Arch Allergy Immunol* 2015;166:150-3.
- Jacobs RL, Andrews CP. Hypersensitivity pneumonia — NSIP histopathological presentation: a study in diagnosis and long-term management. *Ann Allergy Asthma Immunol* 2003;90:265-70.
- Apostolakis MJ, Rossmore H, Beckett WS. Hypersensitivity pneumonitis from ordinary residential exposures. *Environ Health Perspect* 2001;109:979-81.
- Ohtani Y, Ochi J, Mitaka K, Takemura T, Jinta T, Kuramochi J, et al. Chronic summer-type hypersensitivity pneumonitis initially misdiagnosed as idiopathic interstitial pneumonia. *Inter Med* 2008;47:857-62.
- Jacobs RL, Andrews CP, Coalson J. Organic antigen-induced interstitial lung disease: diagnosis and management. *Ann Allergy Asthma Immunol* 2002;88:30-41.
- Hanak V, Golbin JM, Ryu JH. Causes and presenting features in 85 consecutive patients with hypersensitivity pneumonitis. *Mayo Clin Proc* 2007;82:812-6.
- Morell F, Villar A, Montero MA, Munoz X, Colby TV, Pipvath S, et al. Chronic hypersensitivity pneumonitis in patients diagnosed with idiopathic pulmonary fibrosis: a prospective case-cohort study. *Lancet Respir Med* 2013;1:685-94.

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