Author disclosures are available with the text of this letter at www.atsjournals.org.

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Reply to Fernández Pérez

From the Authors:

We appreciate the insightful comments of Dr. Fernández Pérez in reference to our article (1). We agree wholeheartedly that more high-quality evidence is needed in the area of antigen/exposure evaluation in hypersensitivity pneumonia (HP), and in interstitial lung disease more broadly, for that matter.

From a diagnostic standpoint, the results of a recently published Delphi survey suggest that experts in the field highly value a positive exposure history as a diagnostic criterion for HP (2). Indeed, when presented with case scenarios summarizing diagnostic test results, 97.5% of experts selected “confident diagnosis of HP” when the combination of positive environmental exposure history, highly consistent high-resolution computed tomography, highly consistent lung biopsy, and absent alternative diagnosis were presented. In contrast, for a scenario with the same test results but negative environmental exposure history, only 72.5% of experts selected “confident diagnosis of HP” (2).

The idea among expert clinicians that identification of a plausible exposure is a useful diagnostic “test” or criterion is contrasted by evidence that commonly used tests for HP

antibodies/precipitins may be of questionable utility in practice. Millerick-May and colleagues published pilot data after thorough evaluation of the home or workplace environments of 19 patients with HP (3). The protocol involved patient interview using a standardized exposure questionnaire, environmental sampling from the subject’s home/workplace environment, testing of serum for antibodies against a standard (commercial) HP antigen panel and against home/workplace antigens, and identification of a specific antigen when antibodies to home/workplace were found. The questionnaire appears to yield good information on whether exposure is ongoing: seven of eight subjects suspected to have ongoing exposure in the sampled environment had antibodies to environmental antigens. None of the nine subjects not believed to have ongoing antigen exposure reacted to environmental antigens. Crucially, there was little correlation/agreement between antigens identified from the home/workplace and positive results of commercial antigen panels.

These results raise hope that development of an accurate and reliable standardized HP exposure questionnaire is feasible and draw into sharp question the use of commercial antigen panels. Unfortunately for those subjects without identified exposure after questionnaire administration, the pilot protocol appears to provide little additional help in identifying “occult” antigens in the environment. Consensus on diagnosis and classification of HP is indeed sorely needed to move this field forward, ideally with incorporation of emerging high-quality evidence over expert opinion and anecdote when possible. ■

Author disclosures are available with the text of this letter at www.atsjournals.org.

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Originally Published in Press as DOI: 10.1164/rccm.201801-0125LE on March 5, 2018

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Reply to Fernández Pérez

From the Authors:

We appreciate the views shared by Dr. Fernández Pérez and thank him for appreciating the merit of the perspectives on the diagnosis and management of hypersensitivity pneumonitis (HP) by Salisbury and colleagues (1) and by us (2). It was also our intention to provoke further studies in patients with HP and encourage major respiratory societies to assemble a task force to develop clinical practice guidelines and move the field forward. Indeed, Molyneaux and Maher issued a call to arms for the much-needed international consensus on diagnosis and management of HP (3).

We agree with Dr. Fernández Pérez that HP with an array of manifestations on the basis of overlaps of acute and chronic changes in different individual settings poses difficulties in diagnosis, especially when the inciting antigen, the inducer, is not recognized. Despite the lack of a current official consensus on diagnosis, we believe that knowledge in the field of HP increases, and the attempts of different expert groups to propose diagnostic criteria may crystalize into a task force initiative resulting in a statement of a new diagnostic algorithm for HP. We hope that our proposal of a diagnostic algorithm may lead to further studies and to the development of diagnostic criteria for HP by consensus among experts. The differences between our perspective and that of the Michigan group are not substantial; Salisbury and colleagues focused on the fibrotic stage of chronic HP, whereas we covered the overall manifestation of HP (1, 2).

We agree that the definition of “adequate/exhaustive investigation” for the inciting antigen needs to be elaborated. As we have outlined, this is the field where multidisciplinary services—the bedside respiratory clinician, occupational physicist/industrial hygienist, environmental medicine expert, and microbiologist—need to interact and make an accurate diagnosis of HP, an approach of multidisciplinary discussions similar to that recommended based on evidence for the diagnosis of idiopathic pulmonary fibrosis (IPF) (4). Indeed, every physician confronted with patients with a confirmed diagnosis of HP (definite HP) is painfully aware that, despite intense attempts, the source of the inducer may remain unknown. The word “cryptogenic” simply means the etiology/inducer is hidden, and thus we coined the term cryptogenic HP for such patients with HP. This is similar to the term used for organizing pneumonia of unknown etiology (cryptogenic organizing pneumonia). Before the acceptance of the entity IPF, the term cryptogenic fibrosing alveolitis was used for IPF (5). Indeed, we thought very carefully before yielding to the term cryptogenic HP, and, despite being aware of the criticism by peers, we believed that the term cryptogenic HP is apt to describe the situation of truly unknown cause for the HP, rather than calling it idiopathic HP. Besides, the label “cryptogenic” prompts both the patient and the physician confronted with the HP of unknown cause to further investigations in an attempt to look closely for the inciting antigen (6, 7).

Although we are pleased that the American College of Chest Physicians has assembled a task force to develop a multidisciplinary consensus statement to provide recommendations for the diagnosis of HP, we also believe that further initiatives of other major respiratory societies and sponsors will enable evidence-based clinical practice guidelines for diagnosis and management of HP similar to that existing for IPF and will enhance clinical and laboratory research in the field of HP to give this overlooked and underestimated disease the much-needed attention it deserves. Indeed, identifying the inducer for HP is a step in the right direction, leading to better treatment strategies for patients with established HP by avoiding further exposure. It also helps people who are healthy to remain healthy by avoiding exposures to known inducers of HP. Hence, the dictum “prevention is better than cure” for the concern of HP is very appropriate. ■

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Originally Published in Press as DOI: 10.1164/rccm.201802-0314LE on March 5, 2018