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Response

To the Editor:

We thank Sohal et al for their insightful comments in response to the article entitled "The Role of Infection in Interstitial Lung Diseases—A Review"[1] published in this issue of *CHEST*.

Those with chronic lung disease can be susceptible to infection through a variety of mechanisms, including distorted airway/parenchymal architecture and immunosuppressive therapies used to treat underlying diseases; indeed, even the use of inhaled corticosteroids has been implicated in the setting of COPD and asthma.[2] The molecular mechanisms of adherence of these pathogens and how these mechanisms interact with the underlying disease processes, as well as the inhaled or systemic therapies used to treat interstitial lung disease (ILD), are an important avenue of research that needs further attention.

Our review did not find that infectious triggers, commonly implicated in patients with asthma/COPD, were implicated in ILD exacerbations. Specifically, a study looking at *Chlamydia pneumoniae* did not find that this was a common trigger in acute exacerbations of ILD.[3] Additionally, Wootton et al[4] did not find common respiratory pathogens (including rhinovirus) to be a cause for acute exacerbations of idiopathic pulmonary fibrosis; instead, most studies have shown that herpesviruses are more commonly found in the ILD population.[4] These studies, of course, were small, and given the inherent heterogeneity of patients with ILD, firm conclusions cannot be drawn at this time.

Sohal et al point out smoking as yet another contributor putting patients with ILD at risk; this adds yet another layer of complexity, as we do not know the impact of smoking on the progression of idiopathic ILD independent of the natural progression of disease. In healthy individuals, the mucociliary escalator constitutes an important innate pulmonary defense mechanism. Mucociliary dysfunction of the peripheral airways has not been directly shown to cause acute exacerbations of ILD, even though recent studies implicate the mucin gene in the pathogenesis of several ILDs.[5]

It goes without saying that those with chronic lung disease may be vulnerable to infections through a variety of mechanisms. However, little is known about the cause and natural progression of ILDs, and it may be an oversimplification to connect ILDs (especially the idiopathic forms) to other chronic lung diseases such as asthma/COPD. We agree, however, that further research is necessary to elucidate the underlying pathogenesis of ILDs and the molecular mechanisms that lead to acute exacerbations, including the role of infections.

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