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Consequently, a patient with ILD, gastroesophageal reflux disease, and a positive test result for antinuclear antibodies (ANAs) would not have been considered to have ssSSc. ANA positivity can occur in IPF patients, and thus we did not solely rely on this in our analysis. Rather, we highlighted the specificity of nucleolar staining for ANAs.³ In fact, in our previously described cohort of IPF subjects who were anti-Th/To-positive, we argued that, on retrospective analysis, those with ANAs revealed by nucleolar staining, and particularly those with Th/To antibodies, appeared to have had ssSSc-ILD.⁴

Dr. Singh states that antitopoisomerase antibodies have been reported in patients with IPF and suggests this could produce a nucleolar staining ANA. A closer review of the referenced article shows that 18 of 41 IPF patients (44%) had antibodies to DNA topoisomerase II.⁵ However, only 3 of the 18 patients had a positive ANA finding obtained by Hep2 cell substrate, and the pattern of immunofluorescence was not reported. Furthermore, to our knowledge, the presence of antitopoisomerase II antibodies in IPF patients has not been confirmed by another group, although it has been reported in Japanese patients with SSc-ILD.⁶ Additionally, antitopoisomerase II antibodies should not be confused with antitopoisomerase I (anti-Scl-70) antibodies, which are highly specific for diffuse SSc and give a nucleolar pattern on ANA testing. Notably in our study, while all six patients had ANAs revealed by nucleolar staining, only one patient showed antitopoisomerase I (anti-Scl-70) antibodies. We believe that our case definition for ssSSc-ILD accurately differentiates those patients with ssSSc from those with IPF, and that this distinction is clinically useful.

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Oxygen Administration and the Protection of Health-Care Workers From Infections

To the Editor

Hui et al¹ provide a much needed reminder to the medical community that the very oxygen mask that is used to relieve the hypoxia may contribute to the wide dispersal of infected aerosolized particles, and thereby increases the risk of transmission of airborne infection to health-care workers. However, I believe the authors do a disservice by unequivocally declaring that their data allows the demarcation of “a zone of potential aerosol infection with an extra margin of safety.” They would do well to temper this conclusion based on theoretical arguments from a mechanical model with those based on published *in vivo* observations² in humans that clearly demonstrate aerosolized particles traveling, not 30 or 40, but hundreds of centimeters.

The authors conclude that potential infectious patients “should, ideally, be managed in a single, isolation room, under negative pressure. . . .” This type of conclusion simply does not follow from the type of study performed. Furthermore, it is hard to see how managing a contagious patient in a negative-pressure room would provide any protection to a health-care worker. On the other hand, preventing the patients from spraying infectious particles on health-care workers while being administered oxygen, as we have advocated,^{3,4} would provide protection to other patients and health-care workers alike.

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The author is the co-developer of masks described in references 3 and 4 that have been licensed to Viasys Healthcare Inc.

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Response

To the Editor:

We appreciate the comments by Dr. Fisher on our study,¹ which showed a smoke particle dispersion distance of approximately 0.4 m during application of 4 L/min of oxygen via a

simple mask to a human patient simulator. As we pointed out in our article, our human lung model simply reflected a baseline estimate of the distance traveled by any potentially infectious aerosols while the patient was breathing at rest with a respiratory rate of 12 breaths/min. With appropriate references,^{2,3} we have already stressed the importance of full personal protective equipment as an effective infection control measure in protecting health-care workers against severe acute respiratory syndrome.¹

We are well aware of the possibility that viral infection such as severe acute respiratory syndrome has the potential of spreading by an airborne route, and indeed our institution has made a significant contribution to the literature on this issue.^{4,5} It is important for clinicians involved in the management of infectious diseases to understand that environmental factors such as medical ward airflow and ventilation may play a significant role in the aerosol transmission of infection in health-care premises.⁶ In addition to full personal protective equipment and good personal hygiene, the World Health Organization and the Centers for Disease Control and Prevention have recommended in influenza pandemic plans enhanced infection control precautions in health-care facilities, including placing patients with suspected and confirmed H5N1 influenza in negative-pressure isolation rooms with 6 to 12 air exchanges per hour (if available) due to the high lethality of the disease and uncertainty about the mode of human to human transmission.^{7,8} The negative-pressure room will reduce the spread of airborne contamination between rooms, and a recent study⁹ has shown that the air exchange rate and airflow patterns are important factors in the control of airborne virus infection, and good ventilation arrangement may enhance the safety of staff when performing medical treatments within isolation rooms.

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Diagnosing Pleural Effusion

Moving Beyond Transudate-Exudate Separation

To the Editor:

The primary aim of the physician investigating the patient with an undiagnosed pleural effusion is to establish the correct diagnosis with a minimum number of investigations. For > 30 years, the first step in this process is to determine whether the fluid is a transudate or an exudate, which dictates further investigations and management. One consequence of this is the relentless search to find “better” indexes to differentiate transudates from exudates. This letter expresses our view that research efforts directed to this end would be better channeled into identifying disease-specific diagnostic markers.

Simple criteria such as the effusion/serum ratio of protein and lactate dehydrogenase (*ie*, “Light’s criteria”), have proved to be robust in separating transudates from exudates¹ with a diagnostic accuracy of 96%.² This is as near to perfect as is practically possible because the “gold standard” for comparison is clinical diagnosis, which itself carries a small but definite error rate. Even if superior diagnostic criteria were theoretically possible, to establish the superiority of any new proposed criteria over Light’s criteria a sample size of > 13,000 subjects is required (α , 0.05; desired power, 0.90).

Exudates are defined by a higher effusion/serum level of proteins; hence, the levels of most proteins will be higher in exudative effusions, without the proteins necessarily having any specific diagnostic accuracy. Substantial resources can be expended assessing whether a novel marker is a better marker of the transudate-vs-exudate differentiation for little return.

Novel technologies such as global gene profiling and proteomics are now available to improve on this by identifying “fingerprints” for specific diagnoses. Success in this area will help in identifying the cause for an exudate and would be of great clinical value for patients with pleural effusions. We believe that the search for a better marker of a pleural fluid exudate should now be abandoned and that resources should be focused on identifying specific disease markers and improving clinical management.³

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