To the Editor:

We are grateful for the thoughtful commentary by Dr Medford relating to our recent article in CHEST.1 We agree that because procedural risk in patients with idiopathic pulmonary arterial hypertension (IPAH) is high, pretest suspicion for a more ominous diagnosis is warranted prior to invasive studies of associated mediastinal lymphadenopathy (MLAD). Specifically, exclusion of malignancy (lymphoma, lung primary, metastatic primary, and so forth) should be the only immediate justification for invasive assessment in this setting.

Unfortunately, few studies have commented on MLAD associated with pulmonary hypertension. Our observed frequency of close to one in five patients with IPAH (18%) involved a selected cohort with both right-sided heart catheterization and chest CT scan for the purposes of correlating lymphadenopathy with severity of cardiac hemodynamics. This may underestimate the true prevalence of MLAD in all patients with IPAH. We did find a similar distribution and size of abnormal lymph nodes when compared with left-sided congestive adenopathy,2 and, although others have shown resolution or improvement in adenopathy following heart failure treatment,3 only one of nine patients with MLAD and follow-up CT scanning in our study had regression, despite receiving therapy. These specific findings from our study contribute to the clinical understanding of MLAD associated with pulmonary hypertension and may be applicable to MLAD with pulmonary hypertension from other causes.

As Dr Medford noted, enlarged nodes of <2 cm on short axis with known left- or right-sided heart disease may justify observation with directed heart failure management for 1 to 3 months prior to invasive assessment. This approach appears reasonable for MLAD and pulmonary hypertension from most causes. For example, pulmonary hypertension associated with sarcoidosis may be a unifying diagnosis in some patients presenting with persistent MLAD;4 PET scanning and other studies may be suggestive in this setting,5 although sarcoidosis without pulmonary parenchymal findings is unlikely to be immediately life threatening, again justifying a period of observation prior to biopsy assessment if not regressing. There is a known frequent association of MLAD with interstitial lung disease,6 and, as such, diagnostic assessment without other clinical features of malignancy is likely unjustified.

We suggest and agree with a cautious approach to MLAD associated with pulmonary hypertension of any cause, particularly if pretest suspicion for malignancy is low. Further prospective and observational work to refine a safe approach to MLAD in this setting is needed, as noted by Dr Medford.

REFERENCES


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REFERENCES


Air Pollution and Chronic Cough in China

To the Editor:

In a recent issue of CHEST (March 2013), Lai et al. demonstrated that cough variant asthma, upper airway cough syndrome, eosinophilic bronchitis, and atopic cough (AC) constituted the

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DOI: 10.1378/chest.13-0942

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Air Pollution and Chronic Cough in China

To the Editor:

In a recent issue of CHEST (March 2013), Lai et al. demonstrated that cough variant asthma, upper airway cough syndrome, eosinophilic bronchitis, and atopic cough (AC) constituted the
main causes of chronic cough across five regions in China, based on a prospective survey using a modified diagnostic algorithm. They also concluded that geography, seasonality, age, and sex were not related to the spectrum of chronic cough. We do agree with the authors’ viewpoint. However, of note, in developing countries like China one major concern with the environmental factors (haze) should be raised because indoor and outdoor pollutants can cause chronic cough; namely, exposure to pollutants, such as diesel exhaust, sulfur oxides, ozone, nitrogen oxides, and particulate matter; participates in the development of respiratory symptoms. Haze air pollution represents deterioration of the air quality, which is consistently associated with respiratory hospital admissions. Thurston et al. indicated that haze contributed to 24% of respiratory admissions; a 30% increase in outpatient attendance due to haze-related conditions was also observed by Emmanuel et al. after forest fires in Singapore.

In China, haze has become a predominant problem confronted by 1.3 billion people in recent years, especially during the Chinese New Year, when fine particles and gaseous pollutants are released into the atmosphere after intensive displays of fireworks and firecrackers. It seems that the greater the air pollution the higher the prevalence of patients admitted to clinics with chronic cough as the chief complaint. The harmful effect of haze on the lungs may be related to the potential mechanism that particulates sedimentate in the lung, leading to pulmonary damnification and inflammation formation and subsequent reconditioning of the lung. Particulate matter camouflaged in the haze, as a recent value of air quality guidelines for the protection of health, was gradually recognized as a pollutant with significant impact on the pathogenesis of respiratory disease, with evidence of induction of oxidative stress both in vitro and in vivo.

It would be helpful if the authors could investigate the association between particulate matter and chronic cough, to avoid bias introduced by this confounding factor. In addition, 64 cases, accounting for approximately 8.4% of the cohort reported by Lai et al., were diagnosed with unexplained cough, for which haze including particulate matter may be considered as the main cause, incorporating their role in the pathogenesy of chronic cough. Furthermore, subgroup analysis adjusted for daily environmental and meteorologic data across various regions will be appreciated, so as to clarify the causality relationship between environment and chronic cough.

Although the four common causes of chronic cough in the article remain stable across the disparate regions ($\chi^2 = 1.782$, $P > 0.05$) and are in the majority among the potential etiologic factors, the comparison of cough variant asthma ($\chi^2 = 15.902$, $P = 0.003$), upper airway cough syndrome ($\chi^2 = 12.772$, $P = 0.012$), and eosinophilic bronchitis ($\chi^2 = 12.326$, $P = 0.015$) across five regions showed statistical significance, with an overall proportion of 68.4%. Therefore, it is inaccurate to suggest that no association between geography and the spectrum of chronic cough was observed in China.

We thank Dr Mao and colleagues for their interest and comments regarding our recent article in CHEST.1 We agree that air pollution may be associated with cough. In a survey performed in six cities of northeastern China with heavy industrial air pollution, it was found that three air pollutants (total suspended particulates, SO$_2$, NO$_2$) significantly increased the prevalence of persistent cough in children (approximately 21.2%).2 Another study in Hong Kong also showed that exposure to particulate matter in different geographic locations was associated with increased odds of having cough.3 It is reasonable to suppose that haze induces respiratory symptoms including cough. Air pollution is a common problem in China and is usually more serious in winter and spring. Therefore, the prevalence of cough may vary in different seasons because of air pollution, low temperature, and fireworks as mentioned by Dr Mao.

However, our study was focused on the spectrum of causes of chronic cough in the specialist outpatient clinic but not the prevalence of chronic cough in the community. It is difficult to make a subgroup adjusted for air quality data across various regions to clarify its relationship with chronic cough in current cohort groups. A community survey with larger samples is needed in the future to confirm whether there are seasonal or regional differences on the prevalence of chronic cough related to air pollution in China.

Dr Mao pointed out that haze should be the main cause of unexplained cough. In some patients with chronic cough, no cause is identified, leading to the diagnosis of idiopathic cough or unexplained cough, which is often associated with an increased response to tussive agents such as capsaicin. Common cold or influenza are often triggers of chronic cough (including the common causes and unexplained cough) in our experience. It is reported that air pollution exposure clearly exacerbates preexisting bronchial asthma, and sulfur dioxide exposure increases cough response and airway inflammation in guinea pigs. However, there is no study to identify that air pollutants are able to cause chronic cough or increase

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Financial/Nonfinancial Disclosures: The authors have reported to CHEST that no potential conflicts of interest exist with any companies/organizations whose products or services may be discussed in this article.

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Response

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