

**Conflict of Interest Statement:** None of the authors has a financial relationship with a commercial entity that has an interest in the subject of this manuscript.

INGEL K. DEMEDTS  
GUY F. JOOS  
GUY G. BRUSSELLE  
*Ghent University Hospital  
Ghent, Belgium*

## References

1. Demedts IK, Bracke KR, Pottelberge GV, Testelmans D, Verleden GM, Vermassen FE, Joos GF, Brusselle GG. Accumulation of dendritic cells and increased CCL20 levels in the airways of patients with chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 2007;175:998–1005.
2. Tsoumakidou M, Elston W, Zhu J, Wang Z, Gamble E, Siafakas NM, Barnes NC, Jeffery PK. Cigarette smoking alters bronchial mucosal immunity in asthma. *Am J Respir Crit Care Med* 2007;175:919–925.
3. Zhou LJ, Schwarting R, Smith HM, Tedder TF. A novel cell-surface molecule expressed by human interdigitating reticulum cells, Langerhans cells, and activated lymphocytes is a new member of the Ig superfamily. *J Immunol* 1992;149:735–742.
4. de Saint-Vis B, Vincent J, Vandenabeele S, Vanbervliet B, Pin JJ, it-Yahia S, Patel S, Mattei MG, Bancheau J, Zurawski S, *et al.* A novel lysosome-associated membrane glycoprotein, DC-LAMP, induced upon DC maturation, is transiently expressed in MHC class II compartment. *Immunity* 1998;9:325–336.

## Is Giant Cell Interstitial Pneumonitis Synonymous with Hard Metal Lung Disease?

To the Editor:

The large case series of hard metal disease described by Moriyami and colleagues in their article provides an important source of clinico-pathologic data pertaining to a rare, but important interstitial lung disease (1). The implications of the authors' reported observations from an immunological perspective were highlighted in the erudite editorial by Nemery and Abraham in the same issue (2). There were, however, important epidemiologic inferences to be drawn from this report that are also worthy of comment.

The authors used electron probe microanalysis to assess the elemental content in lung biopsy material from 85 patients with interstitial lung disease "suspected to be of environmental or occupational origin." Although 23 of the 85 biopsies studied (27%) manifest pathologic findings of giant cell interstitial pneumonitis (GIP), the basis for study inclusion (i.e., etiological suspicion of an occupational disease) is not elucidated and may very well have included such histology as one criterion. This would be a reasonable approach, given that GIP has come to be treated as a pathologic finding wholly attributable to hard metal or related cobalt-containing exposures. Indeed, this was the stated rationale for "delisting" GIP as an "idiopathic" pneumonia in the 2002 American Thoracic Society/European Respiratory Society (ATS/ERS) statement on the classification of idiopathic interstitial pneumonias (3).

In that light, the further epidemiologic observation of Moriyama and colleagues is all the more intriguing: of the 23 patients with GIP, 2 (8.7%) had no occupational history of exposure (one was a schoolteacher) and no tungsten or cobalt detectable by probe analysis. A recent case report from India of an office sweeper with GIP but no suspect history also raises the question as to whether sporadic cases of this condition occur that cannot be equated with hard metal lung disease (4). There certainly have been cases of GIP in which an occupational history was atypical, but where metals analysis indicated likely occult cobalt exposure (5). Conversely, a thorough metal analysis can be negative, but nonetheless the occupational or environmental history may be highly suspect, as in the case of a 15-year-old with GIP both of

whose parents had occupational exposure to hard metal (6). Nemery and Abraham argue cogently that we need to fill in our knowledge gaps about hard metal lung disease (2). Until we do so, it may have been premature to banish GIP from the schema of "idiopathic interstitial pneumonias," as was done in the ATS/ERS statement (3).

**Conflict of Interest Statement:** P.D.B. has no financial relationship with a commercial entity that has an interest in the subject of this manuscript.

PAUL D. BLANC  
*University of California, San Francisco  
San Francisco, California*

## References

1. Moriyama H, Kobayashi M, Takada T, Shimizu T, Terada M, Narita J-I, Maruyama M, Watanabe K, Suzuki E, Gejyo F. Two-dimensional analysis of elements and mononuclear cells in hard metal lung disease. *Am J Respir Crit Care Med* 2007;176:70–77.
2. Nemery B, Abraham JL. Hard metal lung disease: still hard to understand. *Am J Respir Crit Care Med* 2007;176:2–3.
3. American Thoracic Society. American Thoracic Society/European Respiratory Society international multidisciplinary consensus classification of the idiopathic interstitial pneumonias. *Am J Respir Crit Care Med* 2002;165:277–304.
4. Menon B, Sharma A, Kripalani J, Jain S. Giant cell interstitial pneumonia in a 60-year-old female without hard metal disease. *Respiration (Herrlisheim)* 2006;73:833–835.
5. Choi JW, Lee KS, Chung MP, Han J, Chung MJ, Park JS. Giant cell interstitial pneumonia: high-resolution CT and pathologic findings in four adult patients. *Am J Radiol* 2005;184:268–272.
6. Kakugawa T, Mukae H, Nagata T, Ishii H, Kaida H, Hayashi T, Suematsu T, Kadota J-I, Kohno S. Giant cell interstitial pneumonia in a 15-year-old boy. *Intern Med* 2002;41:1007–1012.

From the Authors:

We appreciate Dr. Blanc's comments on our article (1). We screened 85 biopsies; tungsten was detected in surgical biopsies from 17 patients and in transbronchial biopsies (TBBs) from three additional patients. Three TBBs were excluded from our study because the pathologists could not make an accurate pathologic diagnosis due to the small size of the TBB. A TBB from an office sweeper without an exposure history was pathologically diagnosed as giant cell interstitial pneumonia (GIP) (2), but we did not include TBB cases. Even though pathologists find giant cells when screening biopsies, they should be careful in making a final diagnosis of GIP, because giant cells are found in other diseases such as viral pneumonia, especially pneumonia due to measles, and sarcoidosis.

We applied an improved technique for element analysis of tissue sections using an electron probe microanalyzer (EPMA) with a wavelength dispersive spectrometer (WDS) (1). This technique has about 10 times higher sensitivity than EPMA with an energy dispersive spectrometer and enabled us to detect tungsten in lung tissue in which the element was not found by the other method (unpublished data; Reference 3). We found two biopsies exhibiting features of GIP with neither tungsten nor cobalt detected in the lung tissue by EPMA-WDS nor a working history in the hard metal industry. Finally, 2 (10.5%) of 19 surgical lung biopsies were thought to be "idiopathic" GIP in our case series.

In addition to EPMA, atomic absorption spectrometry, plasma optical emission mass spectrometry, and ionic coupled plasma emission spectrometry have been used to detect tungsten and cobalt in lung tissue (2, 4, 5). All of these techniques are methods to detect elements in dissolved tissue solution. Using these methods, one cannot see the relationship between elements and the characteristic lesions of GIP, including centrilobular fibrosis and giant cell accumulation within alveolar space; thus, some GIP diagnosed as hard metal lung disease might actually be "idiopathic" GIP.

We agree with Dr. Blanc that “it may have been premature to banish GIP from the schema of ‘idiopathic interstitial pneumonias’” as was done in the 2002 American Thoracic Society/European Respiratory Society statement (6). When we screened lung tissue from patients with suspected occupational lung diseases by EPMA-WDS, we sometimes found elements that have not been thought to cause lung injury, including indium, vanadium, and niobium (unpublished data). “Idiopathic” GIP might be caused by extrinsic elements which are difficult to detect with current techniques.

**Conflict of Interest Statement:** None of the authors has a financial relationship with a commercial entity that has an interest in the subject of this manuscript.

TOSHINORI TAKADA  
HIROSHI MORIYAMA  
FUMITAKE GEJYO  
*Graduate School of Medical and Dental Sciences  
Niigata University  
Niigata, Japan*

## References

1. Moriyama H, Kobayashi M, Takada T, Shimizu T, Terada M, Narita J, Maruyama M, Watanabe K, Suzuki E, Gejyo F. Two-dimensional analysis of elements and mononuclear cells in hard metal lung disease. *Am J Respir Crit Care Med* 2007;176:70–77.
2. Menon B, Sharma A, Kripalani J, Jain S. Giant cell interstitial pneumonia in a 60-year-old female without hard metal exposure. *Respiration (Hertlisheim)* 2006;73:833–835.
3. Ishii H, Umeki K, Yoshikawa H, Kushima H, Hashinaga K, Ohama M, Kishi K, Tokimatsu I, Hiramatsu K, Kadota J. A case of bronchiolitis possibly associated with inhalation of hard metal [in Japanese]. *Nihon Kokyuki Gakkai Zasshi* 2007;45:100–104.
4. Kakugawa T, Mukae H, Nagata T, Ishii H, Kaida H, Hayashi T, Suematsu T, Kadota J, Kohno S. Giant cell interstitial pneumonia in a 15-year-old boy. *Intern Med* 2002;41:1007–1012.
5. Choi JW, Lee KS, Chung MP, Han J, Chung MJ, Park JS. Giant cell interstitial pneumonia: high-resolution CT and pathologic findings in four adult patients. *AJR Am J Roentgenol* 2005;184:268–272.
6. American Thoracic Society; European Respiratory Society. American Thoracic Society/European Respiratory Society international multidisciplinary consensus classification of the idiopathic interstitial pneumonias. *Am J Respir Crit Care Med* 2002;165:277–304.