Serum Lactate Dehydrogenase in Interstitial Lung Disease

To the Editor:

It has been stated that an elevated serum lactate dehydrogenase (LDH) concentration in the setting of diffuse lung disease should suggest the diagnosis of pulmonary alveolar proteinosis or *Pneumocystis carinii* pneumonia. However, we suspected that elevations in serum LDH may be nonspecific and simply reflect diffuse lung injury. We prospectively evaluated 81 patients with various forms of interstitial lung disease; all patients had at least two of the following characteristics: (a) radiographic evidence of bilateral interstitial-alveolar chest infiltrates, (b) static lung volumes <80 percent of predicted, and (c) diffusing capacity for carbon monoxide <75 percent of predicted. In 87 (47 percent) patients a definitive diagnosis was established by biopsy. All patients were followed up for an average of 24 months (range, three to 52 months).

Elevated serum LDH values (>425 U/L) were found in 43 percent of patients. Most of these patients had cryptogenic fibrosing alveolitis, but an elevated serum LDH concentration was also seen in cases of bleomycin pneumonitis, sarcoidosis, lymphoid interstitial pneumonia, and lung disease associated with rheumatoid arthritis and systemic sclerosis. Although a high serum LDH level did not appear useful in predicting the cause of interstitial lung disease, it did appear to have some prognostic value. Of the 46 patients with a normal serum LDH level, only four (9 percent) died within the follow-up period (Fig 1). In contrast, 16 (46 percent) of the patients with a high serum LDH level died (p<0.01). Particularly striking was the mortality rate (83 percent) in patients with a serum LDH concentration greater than 650 U/L (Fig 1).

In summary, we found that an elevated serum LDH concentration was of no help in predicting the cause of interstitial lung disease, but was of unexpected prognostic significance. We suspect that an elevated serum LDH concentration in these patients reflects cellular hypoxia and tissue necrosis, and is a marker of acute and severe lung damage. A high serum LDH level also predicts a poor prognosis in patients with acquired immunodeficiency syndrome and *P. carinii* pneumonia.


Reprint requests: Dr. McFadden, Department of Medicine, St. Joseph's Health Centre, 398 Grosvenor Street, London, Ontario, Canada N6H 4B6

REFERENCES


To the Editor:

The observations of Drs McFadden and Oliphant on serum LDH levels in interstitial lung disease are interesting, but somewhat ambiguous. The study group of 81 patients is not well characterized in that fewer than half the patients had a definitive diagnosis established by biopsy. Was the diagnosis in the remaining patients established by radiologic and physiologic criteria only? The uncertainty of diagnosis in the majority of cases weakens the authors' statement that serum LDH values are not useful in predicting the cause of interstitial lung disease. The authors then analyze the prognostic value of serum LDH for all 81 patients, lumped together, irrespective of specific cause. Such an analysis, by definition, does not distinguish patients with cryptogenic fibrosing alveolitis or lung disease with a poor prognosis from patients with sarcoidosis or other lung diseases. It would be more useful to know the prognostic value of the serum LDH level, or any other serum marker for that matter, in patients within a specific disease category.

The serum LDH level in patients with *Pneumocystis* pneumonia, on the other hand, is a useful prognostic marker, precisely because it is being applied to a single disease. Moreover, the changes in serum LDH levels are also useful prognostically as applied to *Pneumocystis* pneumonia specifically.

The speculation that elevated serum LDH values reflect cellular hypoxia might have been supported by relating the LDH levels to the presence of hypoxemia or a widened alveolar-arterial P02 gradient. Is there a correlation between the degree of hypoxemia and the elevation of serum LDH concentration? Are the patients with LDH values greater than 650 U/L distinctive with respect to degree of hypoxemia? It may be that hypoxemia better correlates with prognosis in specific groups of patients.

Robert L. Smith, M.D., F.C.C.P., New York Veterans Affairs Medical Center, New York