Diagnostic Value of Serum to Pleural Fluid Zinc Ratios In Pleural Effusions

**To the Editor:**

Pleural effusions may develop as a manifestation of a wide variety of disease processes. In most instances, the cause of the effusion becomes apparent from the associated clinical circumstances, diagnostic thoracenteses and/or percutaneous pleural biopsies with cultures, cytologic and/or histologic examinations. However, in about 20 percent of cases the effusions remain undiagnosed after the initial evaluation—20 percent of these effusions are later proven to be malignant. These undiagnosed effusions are important problems for which, at present, there is no readily available diagnostic test to help the clinician decide what course to follow (close observation or thoracotomy).

In order to better differentiate malignant from benign pleural effusions, numerous tumor markers have been assayed. These markers, however, generally either require assays that are not routinely available or have poor sensitivity and/or specificity. Thus, as Bueso et al. have recently pointed out, the search for markers that will allow distinction between benign and malignant pleural effusions will continue to be the object of many investigations.

Zinc is a trace element essential for the growth of all tissues. Zinc, however, has been shown to be concentrated in mouse serosal tumors and malignant pleural effusions in man, although there is some overlap with benign effusions. Conversely, serum zinc levels are often depressed in patients with malignant disease. These observations suggest that determining serum-to-pleural fluid zinc ratios might clear up overlapping isolated serum or pleural fluid values and serve as a marker to distinguish malignant from benign effusions.

Human investigations committee approval for a preliminary feasibility study was obtained to address these considerations. Twelve patients with pleural effusions in whom etiologies were established (seven benign, five malignant) had simultaneous serum and pleural fluid levels determinations using the atomic absorber, and serum-to-pleural fluid zinc ratios were calculated.

In this investigation, overlap was found not only in the ranges of zinc levels in benign (6.09 to 61.81 ng/dl) and malignant pleural fluid (14.65 to 47.68 ng/dl), and in benign (21.87 to 44.21 ng/dl) and malignant serum (16.03 to 35.28 ng/dl), but also in serum to pleural fluid ratios (benign 0.7 to 3.6, malignant 0.5 to 1.5).

Although the sample size is small, the results of this investigation indicate that the use of this ratio is unlikely to be a useful method to differentiate patients with benign pleural effusions from those with malignant. Consequently, physicians must continue to rely on clinical judgment in deciding what course to follow in patients in whom initial evaluations fail to establish a cause.

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**Legionella Pneumonia and AIDS**

**To the Editor:**

Pulmonary infection due to Legionella species in patients with AIDS (either as the sole pathogen or accompanying *Pneumocystis carinii* pneumonia) was frequently noted during the period 1981-83. It has more recently been suggested that Legionella pneumonia is now seldom encountered in AIDS patients.

In 1987, a heterosexual man presented to Brooklyn Veterans Administration Medical Center with shortness of breath, cough, fever and chills. Physical examination revealed a temperature of 101°F, pulse 80/min, blood pressure 140/90 Torr, and respiratory rate 36/min. There was no evidence of weight loss. The patient had significant respiratory distress. The remainder of the physical examination was unremarkable, as were routine hematologic, chemical and urine screening tests. Chest roentgenogram revealed bilateral interstitial infiltrates. Gram-Weigert stain of induced sputum revealed PCP, which was confirmed by bronchoalveolar lavage. Despite treatment with trimethoprim-sulfamethoxazole, the patient failed to improve. Direct fluorescent antibody (DFA) stain of sputum revealed Legionella species. Upon institution of intravenous erythromycin therapy, the patient defervesced, improved and was discharged after three weeks of therapy for both infections.

Cognizant of this case at our affiliated institution, we retrospectively reviewed data gathered at the Kings County Hospital Center. Between January, 1985 and October, 1987 fiberoptic bronchoscopy (with lavage, with or without transbronchial biopsy) was performed in 415 instances because of suspected AIDS-related pulmonary disease. In all patients, an aliquot of bronchoalveolar lavage fluid was submitted for DFA staining for Legionella. Only one patient had a positive DFA stain for Legionella. This patient also had coexistent pulmonary Kaposi's sarcoma.

We concur with the suggestion made by the second NHLBI workshop that Legionella pneumonitis is currently extremely rare in AIDS patients. Thus the routine submission of bronchoalveolar lavage for Legionella DFA staining is not warranted unless the patient is not responding to treatment or if a diagnosis is not initially made. In such cases empiric erythromycin therapy may be indicated until appropriate studies can be performed.

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Bronchoalveolar T-lymphocytosis in HTLV-1-associated Myelopathy

To the Editor:

Chronic progressive spastic paraparesis occurring in tropical areas and southwest Japan is frequently associated with high antibody titers to HTLV-I in serum and cerebrospinal fluid. We recently reported that T-lymphocyte alveolitis occurred in patients with HTLV-1-associated myelopathy (HAM). The presence of such pulmonary lesions was also described by Vertan and associates in patients with HTLV-1-associated tropical spastic paraparesis (HTLV-I-TP). In the present study, bronchoalveolar lavage (BAL) fluid had an increased proportion of lymphocytes in patients with HAM (ten women and three men, 50 ± 17 percent), compared to HTLV-1-negative normal control subjects (ten nonsmoking male volunteers, 14 ± 3 percent). Increased BAL lymphocytes consisted mainly of CD3+ cells (78 ± 17 percent) and CD4+/CD8+ ratios (1.5 ± 0.8) were similar to those of normal control subjects (1.3 ± 0.7). Serum levels of soluble interleukin-2 receptors (IL-2R), a marker of T-cell activation, were significantly elevated in patients with HAM compared to normal control subjects (685 ± 210 vs 286 ± 49 U/ml, p<0.01). Soluble IL-2R levels were detectable in BAL fluid from HAM patients and BAL levels were approximately 13 times higher than those in serum (166 ± 103 vs 18 ± 13 U/mg albumin, p = 0.001). BAL IL-2R levels in HAM patients correlated well with the number of lymphocytes and T-cells in BAL fluid (r = 0.68, p<0.05 and r = 0.64, p<0.05, respectively). These results suggest that T-lymphocytes infiltrating the lungs of HAM patients are activated locally to produce IL-2R.

Our data show that bronchoalveolar T-lymphocytosis occurs in patients with HAM, suggesting that immunologic mechanisms play an important role in the development of pulmonary lesions in HAM.

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Bronchoscopic Aspect of Pulmonary Aspergilloma

To the Editor:

We read with interest the paper by Smith et al reporting a patient in whom pulmonary aspergilloma was visualized and biopsied by flexible fiberoptic bronchoscopy. We would like to report another case similar to the one described by Smith et al also diagnosed this way. In this form of Aspergillus lung disease, clinical diagnosis is usually based on radiologic and immunologic criteria; nevertheless fiberoptic bronchoscopy is a simple, easy procedure for confirmation in some cases.

A 40-year-old man was admitted with high fever and a chest x-ray showing a cavitated consolidation of the right upper lobe. During endoscopic examination with an Olympus B2 fiberoptic bronchoscope, we were able to introduce the tip through the B2b bronche into the cavity. Putrid, purulent debris was seen and removed. Culture showed growing for E coli, but anaerobes, mycobacteria or fungi were not isolated. The patient improved when treated with penicillin and tobramycin, and chest x-ray film revealed a cavity with a crescent-shaped air space. Because serum precipitins were found to be negative, fiberoptic bronchoscopy was newly performed and the cavity entered. A fungus ball was seen (Fig 1) and a biopsy taken. Histopathologic examination showed septic hihape, and aspergilloma was confirmed after right superior lobectomy.

Bronchoscopic visualization of a fungus ball has been rarely reported; in fact, we could only find one other reference in the literature. We also performed fiberoptic bronchoscopy in another eight patients suffering from aspergilloma, but we couldn’t enter the cavity in any of them. We assume it was possible in this case due to the cavity’s size, as in Smith’s patient as well. However, we want to point out that definitive diagnostic findings were obtained only when bacterial superinfection was overcome.

Figure 1. Bronchoscopic aspect of the lung cavity showing a fungus ball.