lular lactoferrin, and accounts for the radioactivity detected by scintillation scanning of the lungs.

We investigated the pulmonary disposition of $^{67}$Ga in patients with pneumocystis pneumonia, which is also associated with increased pulmonary vascular permeability and $^{67}$Ga uptake. We found no significant difference between mean bronchoalveolar lavage transferrin concentrations in patients with pneumocystis pneumonia, associated with pulmonary uptake of $^{67}$Ga, and patients without infection and negative gallium scanning. Furthermore, radioactivity in the bronchoalveolar lavage supernatant was correlated with the presence of neutrophil alveolitis, but not with transferrin concentrations. The extracellular release of lactoferrin, which binds gallium with greater affinity than transferrin, may have accounted for the $^{67}$Ga radioactivity in the lavage supernatant from patients with pneumocystis pneumonia and neutrophil alveolitis.

Thus, determination of pulmonary $^{67}$Ga uptake may not provide an accurate assessment of the permeability of the microvasculature to transferrin, but rather, it may reflect the instability of the $^{67}$Ga-transferrin complex in the presence of neutrophil activation and inflammation.

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To the Editor:

We thank Drs. Smith and Berkowitz for their valuable comments on our paper (Chest 1993; 104:1825-32) describing an increased 1-h pulmonary uptake of IV injected $^{67}$Ga, corrected for blood content in patients after prolonged cardiac surgery with cardiopulmonary bypass (CPB). They question our interpretation that the pulmonary $^{67}$Ga uptake, i.e., the pulmonary leak index (PLI), is a measure of microvascular permeability in the lungs. They suggest that the increased $^{67}$Ga-PLI is not caused by increased microvascular transferrin transport but by increased binding to neutrophils, lactoferrin, or both within the pulmonary microvasculature. This would only be possible if the pulmonary microvascular concentrations would greatly exceed those in systemic blood, which is unlikely for lactoferrin if secreted by activated neutrophils in the pulmonary microvasculature and diluted by the blood stream. Nevertheless, we cannot exclude that activated neutrophils in the pulmonary microvasculature could be responsible in part for the increased $^{67}$Ga-PLI in some of our patients, although viable neutrophils may bind less than 1% of the $^{67}$Ga presented to them in vitro. Indeed, the mechanism of $^{67}$Ga uptake in inflammatory lesions is controversial, although increased microvascular permeability may be the main factor involved, because the accumulation of the radionuclide in these lesions is predominantly extravascular and extracellular. The data by Smith et al. (J Nucl Med 1992; 33:512-15) in Pneumocystis carinii pneumonia with increased $^{67}$Ga uptake in the lungs 24 h after IV injection could indicate increased $^{67}$Ga extravasation in the lungs, since the levels of the radionuclide were elevated in the (acellar fraction of) bronchoalveolar lavage (BAL) fluid. The question remains whether proteins or cells would have been responsible for this increased $^{67}$Ga transport. In BAL fluid, the transferrin concentration was normal and the elevated $^{67}$Ga concentration directly correlated with the neutrophil fraction of cells in the fluid. The normal levels of transferrin in BAL fluid could argue against $^{67}$Ga transport by transferrin, although the transferrin levels may not have reflected transferrin extravasation at the time of $^{67}$Ga injection, as acknowledged by the authors. The transport of $^{67}$Ga could have been caused by increased transport through lactoferrin, which was not measured, or neutrophils, which were elevated in the BAL fluid. Increased transport of $^{67}$Ga through lactoferrin would denote increased protein permeability; increased transport through leukocytes would indicate increased cellular permeability. In either case, $^{67}$Ga accumulation in the alveolar space could have been caused only by a change in the pulmonary microvasculature. Hence, the findings by the authors would not argue against the 1-h $^{67}$Ga-PLI as an index of microvascular changes and increased permeability in the lungs. This idea is reinforced by the recent study of Dauber et al., showing a threefold increase in the PLI, using $^{111}$In-lactoferrin, which more firmly binds to circulating transferrin than $^{67}$Ga after bypass in dogs. Hence, these experimental data agree with our data in man (Chest 1993; 104:1825-32). We recently described a patient with pulmonary edema after cocaine/heroin abuse with a 75% neutrophil count in BAL fluid and a normal $^{67}$Ga-PLI of $\sim 8.5 \times 10^{-5} \cdot \text{min}^{-1}$. Moreover, we found an increased $^{67}$Ga-PLI of 52.4 $\times 10^{-3} \cdot \text{min}^{-1}$ in a leukemic patient who developed ARDS after streptococcal sepsis, 3 days after induction of pancytopenia by chemotherapy, virtually eliminating circulating neutrophils. During recovery of neutrophil numbers in blood to $5.2 \times 10^{9} \cdot \text{L}^{-1}$ and resolution of adult respiratory distress syndrome, the $^{67}$Ga-PLI decreased to $6.6 \times 10^{-3} \cdot \text{min}^{-1}$. These data agree with the observation that $^{67}$Ga accumulates in inflammatory lesions, even in case of prior severe neutropenia. Taken together, these data argue against the idea that neutrophil trapping of $^{67}$Ga caused the elevated $^{67}$Ga-PLI in the lungs of our patients with prolonged CPB-surgery. Nevertheless, the mechanisms underlying the $^{67}$Ga-PLI deserve further study.

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