within 24 h of admission, with reference to our study of children on extracorporeal life support (ECLS), no measures made in the first 48 h after commencement of support predicted eventual outcome. We reported the data from the weaning period because we believed that this may best predict ability to sustain adequate cardiorespiratory function off ECLS. For some patients a measure taken 48 h after commencement was close to the end of the ECLS run, while for others it was less than 10% of the way through total duration of support. We agree that the later a variable becomes predictive of an outcome, the less clinically useful it is likely to be, and the less it is likely to be amenable to manipulation. Therefore, there are several questions to be answered regarding the true clinical worth of gastric tonometry in children on ECLS.

There may be pathophysiologic reasons why gastric tonometry may be more useful in identifying poor tissue perfusion in prolonged ECLS than it is in treating other critically ill children. First, splanchnic perfusion may be compromised during prolonged ECLS, either by the nonpulsatile flow in veno-arterial extracorporeal membrane oxygenator, hypovolemia, inadequate cardiovascular support, or the development of nosocomial sepsis. The second reason may relate to the timing of illness and recovery. In children with sepsis, by the time of ICU admission, there is usually established metabolic acidosis or hypotension, and gastric tonometry is not required to identify that they are very ill. These children then either become more or less cardiovascularly stable with treatment over a short period of time. For children on ECLS, after an initial catastrophic presentation and commencement of ECLS, there may be an apparently stable period for many days. It is possible that during this time there may develop splanchnic hypoperfusion which is manifest as a high DCO, or a low pH.

Relating time of weaning to the time of death, seven children died within 24 h of the weaning trial from ECLS, and five others died 2, 6, 15, 19, and 30 days later. Four of the seven who died within 24 h of the weaning trial had a high DCO, for more than 48 h prior to time of weaning. We agree that some of the splanchnic ischemia we were seeing was part of the dying process, which is unlikely to be amenable to therapy. We addressed the issue of the poor predictive value of lactate. The 95% confidence intervals for the area under the ROC curve for lactate as a predictor of mortality were 0 to 0.61, compared with 0.58 to 1.0 for DCO, 0.74 to 1.0 for pH, and 0.61 to 1.0 for base deficit (Wilcoxon test). The small numbers in this study partly explain the broad confidence intervals. Although bicarbonate was used rarely in these children, diuretics, including furosemide infusions, were often used leading up to the weaning trial in an attempt to remove excess body water. We believe that this was a common cause of metabolic alkalosis in these critically ill children.

We feel that further investigation of the value of gastric tonometry is indicated in children on ECLS, and acknowledge that the numbers in our initial study preclude definite conclusions. Like Drs. Gomersall and Joynt, we have been unable to identify other groups of critically ill patients for which gastric tonometry is a source of useful independent information.

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The Lung Scan Appearances of Tumor Embolization

To the Editor:

I read with interest the case report of Moores and colleagues (April 1997).1 I do not agree that microembolism is necessarily a rare cause of “high probability” perfusion defects. The authors state that “Crane et al reported . . . that scintigrams in patients with tumor embolism are distinctly different [from those with thromboembolic disease] . . . smaller, more numerous . . . peripherally located” etc. The report by Crane and colleagues was of three patients, only one of whom had both a ventilation scan and a postmortem examination in addition to the perfusion study. Thus, in quoting this paper, Moores and colleagues are generalizing essentially on the basis of one patient—hardly enough to justify the use of plurals. The appearances described by Crane and colleagues in 1984 would probably be categorized today as “low probability for pulmonary embolism.” Low probability scans have been associated with angiographically diagnosed pulmonary emboli in up to 30% of cases,2 so these appearances should not be regarded as atypical of thromboembolic disease. I believe that lung scans can be classified with confidence into only two categories: normal and abnormal. In cases of abnormality, the cause of the defects is always a matter of speculation.

Tumor macroembolism and microembolism of the pulmonary arteries is a common occurrence. Abati and colleagues3 found tumor cells in 9 of 21 consecutive pulmonary artery catheter specimens of dyspneic patients known to have cancer. Soares and colleagues4 performed autopsies on 222 consecutive cancer cases and detected arterial tumor embolism in 19 (8.5%) and carcinomatosis lymphangitis in 44 cases (19.8%). The lung scan appearances associated with these phenomena remain to be established. High probability lung scans and pulmonary angiograms have been caused by tumor emboli, even in young, apparently healthy persons who were not recognized to have cancer.5,6 Since we have no reliable method of distinguishing tumor emboli from thrombotic emboli, the frequency of the former is completely unknown. Patients with tumor emboli are frequently inappropriately treated with anticoagulant or thrombolytic drugs. When D-dimer testing becomes a routine part of the evaluation of thromboembolic disease, as it inevitably will, the finding of a normal D-dimer level in a patient with an occluded pulmonary artery might serve as a pointer to possible tumor embolization.

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To the Editor:

I appreciate Dr. Egermayer’s interest in our case report. I think we are in agreement that an abnormal ventilation-perfusion scan is nonspecific and may not always be due to venous thromboembolic disease. This was the purpose of publishing the report.

I disagree with his comments concerning the incidence of “high probability” scintigrams in the presence of tumor microembolism. Sostman and colleagues1 report on two patients with histories of breast cancer who were ultimately found to have diffuse tumor emboli. The lung scintigraim in each case was described as having “multiple subsegmental perfusion defects which delineated the major fissure, the basilar segments, and the lingula”—the so-called “contour” pattern. Green and colleagues2 describe four patients with tumor emboli, all of whom had multiple irregular peripheral defects on their perfusion scans. Four other authors3-6 with a total of 14 patients describe similar perfusion defects. More importantly, although 2 of the 14 scintigrams were labeled “high probability,” none of them revealed a unilateral near absence of flow, as in our case. In Seminars in Nuclear Medicine, Sutter and Stadalnik7 reviewed unilateral absence or near absence of pulmonary perfusion on lung scanning. Though they list over 55 diagnostic possibilities in 39 major categories, ranging from common to uncommon to rare causes, they do not even mention tumor microemboli.

As Dr. Egermayer correctly states, tumor macroembolization and microembolization of the pulmonary arteries are more common than originally thought. In the setting of a known prior malignancy, most practitioners today would probably include lymphangitic spread and tumor emboli in their differential diagnosis of dyspnea or unexplained right heart failure. However, the tumor embolization can be the presenting syndrome in a minority of the patients. It is therefore important to keep this in mind in any patient being evaluated for possible thromboembolic disease, regardless of previous history. Martino and colleagues8 suggest criteria which might lead one to search for nonthromboembolic causes of a high probability perfusion lung scan. First, the persistence of symptoms despite adequate anticoagulation is not usual in pulmonary embolism. Second, a perfusion defect maintained over a prolonged period of time without evidence of adverse clinical outcome suggests an anatomic abnormality, rather than embolic origin. Finally, massive, one-sided perfusion defects warrant the consideration of nonembolic origin. It remains to be seen whether D-dimer testing will be another useful screen for abnormalities of nonthromboembolic origin.

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Pulmonary Alveolar Proteinosis

Lung Transplant or Bone Marrow Transplant?

To the Editor:

We read with interest the report by Parker and Novotny (May 1997)1 regarding the recurrence of pulmonary alveolar proteinosis (PAP) after double lung transplantation. Although the authors acknowledge that the disorder in this case might result from diminished alveolar macrophage function and hypothesize that this might be caused by a primary defect in circulating monocytes, they state that the fundamental cellular alteration has yet to be determined. The molecular defect in a murine model of PAP has been established. It supports the authors’ hypothesis and has a direct bearing on the treatment and outcome of this case.

Mice bearing a homozygous targeted disruption of the granulocyte-macrophage colony-stimulating factor (GM-CSF) gene develop PAP at approximately 1 year of age.2 An identical phenotype has been observed in mice with a targeted disruption of the common beta chain of the GM-CSF receptor (GMR c).3 More recently, defective expression of the GMR c gene has been shown in several human patients with PAP,4 perhaps as a result of germline mutation of the GMR c gene. These data suggest that a subgroup of individuals with idiopathic PAP (perhaps including the patient reported by Parker and Novotny) have a deficiency of GM-CSF or its receptor. Bone marrow transplantation can reverse the lung disease in GMR c mice, thus indicating that this form of PAP is clearly a disorder of bone marrow-derived monocytes.5 Therefore, it is not surprising that PAP might recur after lung transplantation in these cases. This case illustrates the need to consider a congenital defect in GM-CSF signaling as a cause of PAP before lung transplantation.