

memory deficits" (added words are italicized). Our original sentence,<sup>3</sup> though correct, is vague and may lead some readers to infer that Dundee and Pandit studied aspects of memory other than retrograde amnesia.

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### Amrinone in Patients Undergoing Cardiac Surgery

To the Editor:—Bailey *et al.*<sup>1</sup> conducted an excellent study of the pharmacokinetics of amrinone during cardiac surgery. However, I disagree with their conclusions regarding the inadequacy of low-dose amrinone (a 0.75-mg/kg intravenous loading dose and a 10- $\mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$  infusion) for providing inotropic support after cardiopulmonary bypass (CPB).

We<sup>2</sup> administered a loading dose of amrinone 0.75 mg/kg, followed by an infusion of 5  $\mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$  (combined with norepinephrine to maintain afterload), to patients during the immediate post-CPB period. The mean cardiac index increased by 65%. When a second dose of 0.75 mg/kg amrinone was given 30 min later and the infusion rate doubled, no additional increase in cardiac index occurred. We initially studied 7 patients but have since found this regimen to be predictable and effective in more than 200.

The finding that a linear dose relationship exists between plasma concentration and cardiac output in patients with chronic congestive heart failure<sup>3</sup> cannot be extrapolated to patients needing inotropic support immediately after CPB. Postbypass myocardial dysfunction is multifactorial, acute, and unpredictable with respect to severity. The plasma concentration of 1.7  $\mu\text{g}/\text{ml}$  is considered by some to be a threshold therapeutic level in a stable environment. However, blood levels and, presumably, intracellular levels are likely to fluctuate in the postbypass phase of hemodynamic instability and cannot be depended on to serve as rational guides to dosage choice.

Wilson *et al.*<sup>4</sup> demonstrated a counterclockwise hysteresis in patients with chronic congestive heart failure when cardiac index, corrected for baseline values, was plotted as a function of plasma concentration of amrinone. They observed a lack of concordance between the time course of changes in cardiac index and plasma concentration. The authors suggested that the site of action of amrinone is pharmacokinetically distinguishable from the plasma and from the tissues in instantaneous equilibrium with the plasma. The instability of the immediate post-CPB state would certainly enhance the disjunction between plasma levels and response to amrinone.

Bailey *et al.* incorrectly cited the work of Butterworth *et al.*<sup>5</sup> to support their conclusion that low-dose amrinone is inadequate in the immediate postbypass phase. The study described in the abstract of Butterworth *et al.* was done 24–36 h postoperatively and has little relevance to the optimal dosage in the immediate postbypass period.

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In Reply:—We agree with Lathi that the relationship between amrinone plasma levels and therapeutic effect in cardiac surgical patients

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Clearly, multiple factors affect heart function at separation from CPB. The appropriate dose of amrinone in patients separating from CPB is best determined by examining the therapeutic end-points of improved hemodynamic characteristics and cardiac indices. Although knowledge of pharmacokinetics is useful, we must avoid treating a blood level and remember that more is not necessarily better.

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immediately after cardiopulmonary bypass is unknown. A controlled study of this question is certainly needed. However, we do not believe