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An Additional Concern with Respect to Patient-controlled Analgesia

To the Editor:—We recently have undertaken a survey of the visitors of patients who were receiving patient-controlled analgesia (PCA) after surgery to determine their understanding of the system. Upon being seen on rounds by the Acute Pain Service, the visitors of 30 patients were asked two questions: 1) "Do you know the function of this button?" (*i.e.*, the hand-held device that the patient depresses to receive a dose), and 2) "If the patient were asleep but looked like he/she was in pain, would you push the button for him/her?"

Twenty-six of the 30 respondents correctly identified the button; of these, 14 indicated that they would push the button to deliver a dose of analgesic if the patient appeared to be in pain. After being informed of the button's function, 2 of the 4 remaining visitors likewise said they would press it for the patient.

We believe that this potentially negates one of the safety features of PCA, namely, that the patient must be awake in order to depress the button. Although we know of no complications to date, we nevertheless believe that it is important to inform visitors appropriately. Perhaps it would be reasonable to place a label on each PCA device indicating that "this button is to be pushed by the patient only." An appreciation of the potential problem may be of vital importance, especially as hospitals hurry to comply with recommendations that techniques such as PCA be used to provide postoperative analgesia (*i.e.*, the new Guidelines for Postoperative Pain Management prepared by the United States Agency for Health Care Policy and Research of the Department of Health and Human Services).

MATHEW THRAN, M.D.
DAVID G. SILVERMAN, M.D.
Department of Anesthesiology
Yale University School of Medicine
P.O. Box 3333
333 Cedar Street
New Haven, Connecticut 06510

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Anterograde, Not Retrograde, Amnesia after Thiopental

To the Editor:—Ghoneim and Block,[1] in their review article "Learning and Consciousness during General Anesthesia," have misquoted the conclusions of our paper[2] regarding the amnesic properties of thiopental, which leads to an entirely confusing impression on the subject. They state, "Although Dundee and Pandit have suggested that both thiopental (6 mg/kg) and methohexital (4 mg/kg) have little effect on memory, definitive study with thiopental using a paired associate task showed impairment."[3] One cannot compare the two studies, because whereas we[2] studied the retrograde amnesic properties of various intravenous anesthetics, Osborn and coauthors[3] studied the anterograde amnesic effects of thiopental. One must differentiate between the two types of amnesia (anterograde *vs.* retrograde) while discussing the drug effects. In our study, we found that not only did thiopental 6 mg/kg and methohexital 4 mg/kg produce no retrograde amnesia, even diazepam 1 mg/kg and propanidid 4 mg/kg did not produce any retrograde amnesia. This is because, it is well known that these agents will produce varying degrees of anterograde amnesia in a dose-dependent fashion. I hope this explanation will clear the misunderstanding that some readers may have after reading Ghoneim and Block's excellent article.

SUJIT K. PANDIT, M.D.
Department of Anesthesiology
University of Michigan Medical Center
IG323 University Hospital
1500 East Medical Center Drive
Ann Arbor, Michigan 48109-0048

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In Reply:—Pandit is correct in directing our attention to the fact that he and the late Dundee were looking only for retrograde amnesic effects in the study cited.[1] Osborn *et al.*,[2] in a particularly analytical study, examined various aspects of learning and memory under the influence of thiopental. They found that while most of the memory impairment could be attributed to acquisition and retention, there was some evidence that retrieval also was impaired. In terms of anterograde and retrograde types of memories, the amnesia was anterograde but not retrograde. In retrospect, we should have written "*While* Dundee and Pandit have suggested that both thiopental and methohexital have little effect on memory *for information acquired before treatment,* a definitive study with thiopental using a paired associate task showed *various*

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

M. M. GHONEIM, M.D.
R. I. BLOCK, PH.D.
Department of Anesthesia, College of Medicine
The University of Iowa
Iowa City, Iowa 52242

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Amrinone in Patients Undergoing Cardiac Surgery

To the Editor:—Bailey *et al.*[1] 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-$\mu g \cdot kg^{-1} \cdot min^{-1}$ infusion) for providing inotropic support after cardiopulmonary bypass (CPB).

We[2] administered a loading dose of amrinone 0.75 mg/kg, followed by an infusion of 5 $\mu g \cdot kg^{-1} \cdot min^{-1}$ (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[3] 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 $\mu g/ml$ 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.*[4] 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.*[5] 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.

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.

KISHOR G. LATHI, M.D.
Assistant Professor
Tufts University School of Medicine
Department of Anesthesiology
St. Elizabeth's Hospital of Boston
736 Cambridge Street
Boston, Massachusetts 02135

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In Reply:—We agree with Lathi that the relationship between amrinone plasma levels and therapeutic effect in cardiac surgical patients immediately after cardiopulmonary bypass is unknown. A controlled study of this question is certainly needed. However, we do not believe