

However, to avoid situations such as this in the future, we have changed the product insert for all new products manufactured and will provide dead-end caps with the set. The product labeling will indicate to "replace caps on valves when not in use."

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Should Calcium Be Administered Prior to Separation from Cardiopulmonary Bypass?

To the Editor:—Robertie *et al.*¹ provide an excellent study on the changes in calcium homeostasis observed during cardiopulmonary bypass. However, the data do not support their conclusion that administration of calcium during attempts at separation from bypass is unnecessary and potentially harmful. The authors point out that a change of 0.07 mM of ionized calcium (Ca_i) will elicit a maximal parathyroid hormone response. Prior to separation from bypass, the authors observed a decrease in Ca_i of over double this value when compared with the prebypass value but report this as a return to "near-normal." It seems that such a difference has significant physiologic implications. The reference cited relating deleterious effects of Ca_i in the setting of ischemia also implicates oxygen free radical formation as a major component in reperfusion injury.² In fact, reperfusion injury responds favorably to agents such as catecholamines that increase intracellular calcium.

A point often overlooked is that the bulk of calcium influx and free radical formation occurs within the first few minutes after reperfusion and is complete within 10 min.²⁻⁴ Administration of calcium prior to separation from bypass occurs long after removal of the aortic clamp and is unlikely to contribute in any significant way to reperfusion injury. Correction of Ca_i after bypass has been demonstrated to significantly improve left ventricular compliance and enhance myocardial performance.⁵ The inhibitory effect of calcium on epinephrine cited by the authors was observed in normocalcemic patients rendered hypercalcemic and was recorded 24 h after surgery.⁶ It seems logical to achieve normocalcemia prior to separation from bypass before administering catecholamines whose mechanism of action involves enhanced intracellular transport of calcium. A pump works most efficiently when properly primed.

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In Reply:—We thank Hosking for his comments about our study.¹ We did not intend to give readers the impression that we totally oppose administration of calcium salts upon emergence from cardiopulmonary bypass. Rather, we believe that the routine administration of calcium salts is unwarranted. In a hemodynamically unstable and severely hypocalcemic patient (ionized calcium concentration < 0.8 mM), we would administer calcium salts (guided by frequent measurements of the ionized calcium concentration in blood) to restore normocalcemia. Likewise, calcium salt administration is appropriate therapy for severe hyperkalemia.

In our study, we observed a return of ionized calcium concentrations to near-normal values prior to separation from bypass. The precipitous decline in parathormone concentrations that we measured simultaneously confirms that these ionized calcium concentrations are near normal. Nonetheless, we do not know the optimal ionized calcium concentration for critically ill patients. For example, animals given en-

dotoxin have improved survival with hypocalcemia compared to either normocalcemia or hypercalcemia.²

We believe that hypercalcemia is dangerous and should be avoided. In addition to the concerns that we cited in our paper (lack of efficacy of calcium at stimulating cardiac output,³⁻⁵ inhibition by calcium of the actions of both epinephrine⁴ and dobutamine,⁶ and the importance of calcium ions in reperfusion injury,⁷ a recent study⁸ has identified therapeutic hypercalcemia (from overzealous calcium salt administration to cardiac surgery patients) as a risk factor for the development of perioperative pancreatitis. In addition, increased intracellular calcium ion concentration is associated with delayed after-depolarizations, a frequent mechanism of postischemic arrhythmias.⁹ In fact, hypocalcemia has been used in the past as a treatment for these arrhythmias.¹⁰

Cardiac ischemia is not terminated when the clamp is released, as is implied by Hosking. Smith *et al.* have documented a higher incidence of cardiac ischemia after separation from bypass than before bypass.¹¹

Hosking cites the study by Yokoyama *et al.*¹² as evidence that calcium administration enhances myocardial performance. Yokoyama and his colleagues decreased the ionized calcium concentration to less than 50% of the normal control value (far less than the concentrations we measured immediately prior to separation from bypass) before administering calcium salts. Toxic hypocalcemia may lead to impaired myocardial performance amenable to improvement by administration of calcium salt.¹³ We do not believe that the study by Yokoyama *et al.* offers evidence that calcium salts may be safely and efficaciously administered to nearly-normocalcemic patients emerging from extracorporeal perfusion. A more recent study from the same group confirms the deleterious effects of calcium after ischemia.¹⁴

Hosking asserts that "it seems logical to achieve normocalcemia prior to separation from bypass before administering catecholamines whose mechanism of action involves enhanced intracellular transport of calcium." We know of no data supporting a reduced efficacy of catecholamines in moderately hypocalcemic patients. Indeed, we have recently observed that moderately hypocalcemic patients respond normally to epinephrine at the time of separation from cardiopulmonary bypass.⁵ In current studies in our laboratory, we have measured no reduction in the ability of epinephrine to stimulate cyclic AMP production until ionized calcium concentrations decrease to less than 0.5 mM. However, we have measured reductions in the efficacy of inotropic agents following calcium administration *in vitro* (studies in progress), in whole animals,^{15,16} and in patients.^{4,6}

In summary, we stand by our conclusions that calcium salts lack efficacy at increasing cardiac output and that their routine administration be avoided in the reperfused, ischemic heart. Until outcome studies demonstrate that routine calcium administration is a safe practice, we will reserve calcium administration for those patients with specific indications.

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Postintubation Croup in Children

To the Editor:—Postintubation croup is a commonly cited problem occurring in healthy children after anesthesia. A prospective study by

Koka, et al,¹ demonstrated an overall incidence of 1% and identified several factors that were positively correlated with the occurrence of