by fluid resuscitation as they are the result of both a decrease in systemic vascular resistance and a negative inotropic effect. By no means are these side effects negligible, and we therefore would like to advise our colleagues to use propofol with the utmost care in patients with cardiovascular disease, peripheral vascular disease, and those with hypovolemia.

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Propofol Causes Cardiovascular Depression. III.

To the Editor:—In the recent review of propofol,[1] Sebel and Lowdon stated that administration of propofol to patients with good left ventricular function undergoing myocardial revascularization was reported to cause consistent, significant decreases in blood pressure, variable changes in heart rate, and no statistically significant changes in cardiac output or cardiac index. These data were obtained from earlier European reports, but Kaplan *et al.** found that even in patients with good left ventricular function (ejection fractions of 30% or better and no previous myocardial infarctions within 3 months of their study), propofol produced significant decreases in MAP, SVR, and LVSWI as well as an increase in heart rate. The addition of other agents during anesthesia (halothane and pancuronium) further accentuated these effects prior to intubation. The authors indicated that their results imply that these decreases may be due to some degree of myocardial depression in addition to some vasodilatory effect. Lippmann *et al.*† found noncardiac elective surgical patients (ASA physical status 2–3) that LVSWI decreased by 35%, cardiac index by 18%, and MAP by 23%, respectively, with no significant decreases in PVR and SVR. Heart rate remained stable. Other studies,[2] also showed the cardiodepressant effect of propofol.

Further in their article, Sebel and Lowdon[1] stated that administration of propofol in combination with a potent opioid may constitute "safer practice" and offer more effective blunting of autonomic sympathetic responses. This may be correct in managing the hypertensive reaction to laryngoscopy in most patients but not in the poor-risk patient, patients with poor cardiac reserve, or even in patients about to undergo cardiac surgery with good left ventricular function. Vermeyen *et al.*[3] in their investigations found that propofol depressed the heart and the addition of fentanyl accentuated this depressant effect. Therefore, the combination of potent opioid with propofol does not offer a "safer practice" and should be used with due caution. The cardiovascular depressant effects of propofol must be borne in mind when this drug is being used in clinical practice.

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* Kaplan JA, Guffin AV, Mikula S, Dolman J, Profeta J: Comparative hemodynamic effects of propofol and thiamylal sodium during anesthetic induction for myocardial revascularization. Journal of Cardiothoracic Anesthesia 2:297–302, 1988.

† Lippmann M, Paicius R, Gingerich S: A controlled study of the hemodynamic effects of propofol vs thiopental during anesthesia induction. Seminars in Anesthesia 7:116–122, 1988.

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In Reply:—We agree with Dr. Van Aken that the reports on the cardiovascular system are conflicting, and we agree with all three letters that anesthesia with propofol can be associated with marked reductions in cardiac output, a finding generally supported by much of the literature published since our review was written.

Drs. Merin and Van Aken raise an interesting point when they suggest that in the studies where cardiac output is not affected, there is significant respiratory acidosis. In the study by Claeys *et al.*,[1] although the *p*H fell from 7.38 to 7.30 (mean), the arterial P_{CO_2} increased from 38 mmHg to only 42 mmHg (mean) while the subjects were breathing room air. On the other hand, and as Dr. Merin states, Stephan *et al.*[2] found that hypercarbia resulted in no depression of cardiac output compared with awake controls, while normocarbia and hypocarbia resulted in significant (15%) decreases in cardiac output. While respiratory status is undoubtedly one factor modifying the cardiovascular effects of propofol, other factors such as pre-existing disease state and medications, intravascular volume status, and other anesthetics are also relevant. For example, nitrous oxide is known to cause cardiovascular depression in combination with other anesthetics,[3] although this has been shown not to be an important effect following a single induction dose of propofol.[4]

Most authors agree that propofol has a vasodilating effect and that systemic vascular resistance (SVR) is decreased,[5,6,*] although Van Aken's group found major effects on cardiac output and stroke volume but only minor effects on SVR[7] or an increase in SVR with intubation.[4] Lepage *et al.*[8] also found the reduction in arterial pressure following propofol alone to be related entirely to a decrease in cardiac index and preload, with SVR remaining unchanged. In an open-chested pig model, propofol was found to produce a dose-related decrease in myocardial contractility associated with an increase in SVR.[9] There appears to be no way to reconcile these different findings. Similar anesthetic protocols have been used, generally resulting in a decrease in SVR, yet in a limited number of studies, SVR is unchanged or increased.

Both Van Aken and Lippmann and Mok comment on our statement that "propofol in combination with an opioid may constitute safer practice and offer more effective blunting of autonomic sympathetic responses." This statement related to the study of Stephan *et al.*[6] in which myocardial lactate production was found using propofol alone but when fentanyl was added and surgery was started, myocardial blood flow, arterial pressure, and heart rate returned towards baseline. These results were confounded by surgical stimulation. The recent data of Van Aken *et al.*[7] and Lepage *et al.*[8] suggest that the addition of fentanyl to either a bolus dose or an infusion of propofol results in deleterious cardiovascular effects.

In summary, although the circumstances under which SVR and cardiac output are affected remain to be fully elucidated, a marked decrease in arterial pressure is a universal finding after induction with propofol. The cardiovascular effects of this drug are, as the authors of the three letters point out, more pronounced than those following the usual iv anesthetic agents.

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