Anesthesiology
75:377, 1991

In Reply:—Buffington suggests that the experimental model we used[1] and the model he used in a previous study[2] are similar. In fact, they are quite different. In the previous investigation by Buffington *et al.*, a baseline anesthetic (not "sedation") of morphine and chloralose was used.[2] The presence of any baseline anesthetic certainly has the potential of altering hemodynamic actions to superimposed isoflurane. This may be especially true for chloralose (an anesthetic we usually avoid because it produces metabolic acidosis). Our investigation was completed in chronically instrumented dogs with control observations made in the awake, unsedated state. Coronary blood flow was allowed to vary naturally in our experiments. Buffington *et al.*[2] controlled total flow through the left main coronary artery with a pump. In our investigation, collateral-dependent, stenotic, and normal regions were present. In the study by Buffington *et al.*, only stenotic and collateral-dependent zones were studied. No normal area was present: the "normal" zone had flow reduced by a pump and thus was similar to a region distal to a severe stenosis. Careful analysis of Dr. Buffington's work[2] (fig. 4) indicates that no significant increase in myocardial blood flow as measured by the radioactive microsphere technique occurred in the "normal" (actually stenotic) zone and that no significant decrease occurred in the collateral-dependent zone during isoflurane anesthesia. Because of small changes in collateral-dependent and "normal" zone flows, however, the ratio of perfusion between collateral-dependent and "normal" zones was slightly reduced in one of the several protocols. In our investigation, we calculated collateral-dependent to stenotic zone flow ratios as well as collateral-dependent to normal zone flow ratios and found no evidence of coronary steal with isoflurane. In contrast, adenosine produced a marked steal of collateral flow in our model.

Nevertheless, in our investigation, no increase in myocardial blood flow in a truly normal zone was observed during administration of isoflurane anesthesia. This was no surprise. The study conducted by Moffitt *et al.*[3] (referred to by Buffington in his letter) measuring coronary sinus blood flow in patients was unable to demonstrate an increase in coronary blood flow during isoflurane anesthesia. These investigators did find a small reduction in calculated coronary vascular resistance but only at one point during induction of anesthesia with isoflurane and *thiopental.* The decrease in coronary vascular resistance occurred concomitant with an increase in heart rate and a decrease in arterial pressure. Coronary steal, by definition, occurs independently of changes in systemic hemodynamics. Therefore, from Moffitt *et al.*'s clinical study, proof that "isoflurane does cause coronary dilation in humans" is debatable at best.

We are in total agreement with Buffington's comment that if coronary vasodilation does not exist to a significant degree, coronary steal will not occur. This appears to be the case for isoflurane. This agent certainly is not a potent coronary vasodilator compared to other drugs (adenosine, chromonar, and dipyridamole), which are known to cause steal.[4–7] *In vitro,* isoflurane does have direct actions to relax coronary vascular smooth muscle.[8] *In vivo,* however, isoflurane also possesses indirect actions (such as a decrease in inotropic state and reduction of afterload) that reduce myocardial oxygen consumption and increase coronary vascular resistance through metabolic autoregulation. The latter actions offset any weak direct coronary vasodilator effect. These mechanisms may explain the minimal change in coronary blood flow during isoflurane *in vivo,* and, in the absence of any significant coronary dilation, no coronary steal will be observed.

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What Is the Mechanism of Action of Aprotinin?

To the Editor:—Although we compliment Dietrich *et al.*[1] on a much-needed clinical study describing the effect of high-dose aprotinin in patients undergoing myocardial revascularization, we believe that the data presented are insufficient to support the authors' conclusions regarding the mechanism(s) by which aprotinin reduces postoperative blood loss.